

533 Rec'd PCT/PTO 17 SEP 2001

FORM PTO-1390 (Modified) (REV 11-2000)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTORNEY'S DOCKET NUMBER GKS-101.0 (7911/83687)	
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371				U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR 09/936852	
INTERNATIONAL APPLICATION NO. PCT/EP00/02410		INTERNATIONAL FILING DATE March 17, 2000		PRIORITY DATE CLAIMED March 17, 1999	
TITLE OF INVENTION NUCLEIC ACID MOLECULE COMPRISING A NUCLEIC ACID SEQUENCE CODING FOR A HAEMOCYANIN					
APPLICANT(S) FOR DO/EO/US Jurgen MARKL, Benjamin ALTENHEIN, Bernhard LIEB and Thomas STIEFEL					
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:					
<ol style="list-style-type: none"> 1. <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C. 371. 2. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371. 3. <input type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (24) indicated below. 4. <input type="checkbox"/> The US has been elected by the expiration of 19 months from the priority date (Article 31). 5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371 (c) (2)) <ol style="list-style-type: none"> a. <input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau). b. <input checked="" type="checkbox"/> has been communicated by the International Bureau. c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US). 6. <input checked="" type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)). <ol style="list-style-type: none"> a. <input checked="" type="checkbox"/> is attached hereto. b. <input type="checkbox"/> has been previously submitted under 35 U.S.C. 154(d)(4). 7. <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3)) <ol style="list-style-type: none"> a. <input checked="" type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau). b. <input type="checkbox"/> have been communicated by the International Bureau. c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. d. <input type="checkbox"/> have not been made and will not be made. 8. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). 9. <input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)). 10. <input type="checkbox"/> An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)). 11. <input type="checkbox"/> A copy of the International Preliminary Examination Report (PCT/IPEA/409). 12. <input type="checkbox"/> A copy of the International Search Report (PCT/ISA/210). <p>Items 13 to 20 below concern document(s) or information included:</p> <ol style="list-style-type: none"> 13. <input type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98. 14. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included. 15. <input checked="" type="checkbox"/> A FIRST preliminary amendment. 16. <input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment. 17. <input type="checkbox"/> A substitute specification. 18. <input type="checkbox"/> A change of power of attorney and/or address letter. 19. <input checked="" type="checkbox"/> A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825. 20. <input type="checkbox"/> A second copy of the published international application under 35 U.S.C. 154(d)(4). 21. <input type="checkbox"/> A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4). 22. <input checked="" type="checkbox"/> Certificate of Mailing by Express Mail 23. <input type="checkbox"/> Other items or information: 					

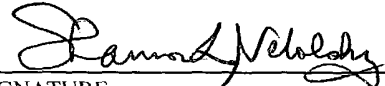
U.S. APPLICATION NO. (IF KNOWN) SEE 37 CFR 09/936852	INTERNATIONAL APPLICATION NO. PCT/EP00/02410	ATTORNEY'S DOCKET NUMBER GKS-101.0 (7911/83687)
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24. The following fees are submitted:				CALCULATIONS PTO USE ONLY	
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :					
<input type="checkbox"/> Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO			\$1000.00		
<input checked="" type="checkbox"/> International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO			\$860.00		
<input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO			\$710.00		
<input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4)			\$690.00		
<input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4)			\$100.00		
ENTER APPROPRIATE BASIC FEE AMOUNT =				\$860.00	
Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).				\$0.00	
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	44 - 20 =	24	x \$18.00	\$432.00	
Independent claims	11 - 3 =	8	x \$80.00	\$640.00	
Multiple Dependent Claims (check if applicable). <input type="checkbox"/>				\$0.00	
TOTAL OF ABOVE CALCULATIONS =				\$1,932.00	
<input type="checkbox"/> Applicant claims small entity status. (See 37 CFR 1.27). The fees indicated above are reduced by 1/2.				\$0.00	
SUBTOTAL =				\$1,932.00	
Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492 (f)).				\$0.00	
TOTAL NATIONAL FEE =				\$1,932.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31) (check if applicable). <input type="checkbox"/>				\$0.00	
TOTAL FEES ENCLOSED =				\$1,932.00	
				Amount to be: refunded	\$
				charged	\$

- a. ☒ A check in the amount of \$1,932.00 to cover the above fees is enclosed.
- b. ☐ Please charge my Deposit Account No. _____ in the amount of _____ to cover the above fees. A duplicate copy of this sheet is enclosed.
- c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 23-0920 A duplicate copy of this sheet is enclosed.
- d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:


SIGNATURE

Shannon L. Nebolsky
NAME

41,217
REGISTRATION NUMBER

September 17, 2001
DATE

09/936852

JC12 Rec'd PCT/PTO 17 SEP 2001

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Jürgen MARKL, et al.)
Serial No.: Not yet assigned) Attorney Docket:
Filing Date: September 17, 2001) GKS-101.0
For: NUCLEIC ACID MOLECULE) 7911/83687
COMPRISING A NUCLEIC ACID)
SEQUENCE CODING FOR A)
HAEMOCYANIN)
Examiner: Not yet assigned) Group Art Unit:
Not yet assigned)

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

This paper is a Preliminary Amendment for the U.S. national phase filing of PCT/EP00/02410 filed herewith as a new patent application under 35 U.S.C. § 371. Please enter this Preliminary Amendment and amend the accompanying application as follows.

New §371 Application
Based on PCT/EP00/02410
Filed August 17, 2001
Markl, et al.

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IN THE ABSTRACT:

Please cancel the Abstract section that was originally filed, entitled "Abstract" and substitute the new ABSTRACT.

- -ABSTRACT

The present invention relates to a nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a fragment thereof with the immunological properties of at least one domain of haemocyanin. The invention furthermore relates to constructs which comprise the nucleic acid molecule and, where appropriate, a promoter suitable for expression control. In a preferred embodiment, the construct furthermore comprises a nucleic acid sequence which codes for an antigen. The invention moreover relates to host cells which contain these nucleic acid molecules and/or constructs. The invention furthermore relates to recombinant expression of the nucleic acid molecules and/or constructs in the host cells. The invention furthermore relates to haemocyanin, a haemocyanin domain, a fragment with the immunological properties of at least one domain of haemocyanin and haemocyanin fusion proteins, which are coded by the nucleic acid molecules and/or constructs. The invention furthermore relates to pharmaceutical compositions which comprise the nucleic acid molecules and/or haemocyanin, a haemocyanin domain, a fragment thereof or a fusion protein. The invention furthermore relates to liposomes which comprise the nucleic acid molecules and/or haemocyanin, a haemocyanin domain, a fragment

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thereof or a fusion protein. The invention furthermore relates to antibodies which are obtainable by immunization of a test animal with haemocyanin, a haemocyanin domain, a fragment thereof or a fusion protein, and the use thereof in screening methods for the identification of tumours.--

IN THE CLAIMS

Please cancel Claims 1 through 44 and substitute new Claims 1 through 44.

REMARKS

Prosecution and consideration of the claimed subject matter in the accompanying patent application is respectfully requested.

I. The Amendments

The attached English translation of the claims as filed in the corresponding international patent application were amended to conform to standard U.S. practice. As a result, the originally-filed English translation of Claims 1 through 44 were cancelled and replaced with the substitute Claims 1 through 44.

A copy of the claims showing the amendments effected by this substitution of the claims is enclosed. The substitute

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claims derive their support from the claims as originally filed with amendments as to form rather than substance.

Claims 1-44 are in the case and are before the Examiner. It is thus seen that no new matter has been presented. A complete, clean copy of the claims before the Examiner is enclosed herewith.

SUMMARY

The Abstract and the claims were amended to conform to standard U.S. practice.

The application is believed to be in condition for allowance. An early notice to that effect is earnestly solicited.

A filing fee is enclosed based on the number of independent and dependent claims in the application after entry of this Preliminary Amendment. No further fee or petition is believed to be necessary. However, should any further fee be needed, please charge our Deposit Account No. 23-0920, and deem this paper to be the required petition.

The Examiner is requested to phone the undersigned should any questions arise that can be dealt with over the phone to expedite this prosecution.

Respectfully submitted,


Shannon L. Nebolsky, Reg. No. 41,217

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CERTIFICATE OF EXPRESS MAILING

I hereby certify that this Preliminary Amendment including clean and marked-up copies of the Amendments, together with a 371 application and its papers and fee, are being deposited with the United States Postal Service as Express Mail Label No. EL706574854US, postage prepaid, in an envelope addressed to: Commissioner for Patents, Box PCT, Washington, D.C. 20231 on September 17, 2001.

Frank Jones

**Nucleic acid molecule comprising a
nucleic acid sequence which codes for a haemocyanin**

The present invention relates to a nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a fragment with the immunological properties of at least one domain of haemocyanin, constructs which comprise this, host cells which comprise the nucleic acid sequences or the constructs, processes for the preparation of haemocyanin polypeptides, and recombinant haemocyanin polypeptides.

Haemocyanin is a blue copper protein which occurs in a freely dissolved form in the blood of numerous molluscs and arthropods and transports oxygen. Of the molluscs, the cephalopods, chitons, most gastropods and some bivalves contain haemocyanin. Among the arthropods, haemocyanin is typical of arachnids, xiphosurans, malacostracan crustaceans and *Scutigera*. Numerous species of insects contain proteins which are derived from haemocyanin. Haemocyanins are present in the extracellular medium and float in the haemolymph.

While arthropod haemocyanin has a maximum diameter of 25 nm under an electron microscope and a subunit has a molecular weight of 75,000 Da, mollusc cyanins are much larger. Thus e.g. the haemocyanin of *Megathura* has a diameter of 35 nm and is composed of 2 subunits. Each subunit has a molecular weight of approx. 400,000 Da and is divided into eight oxygen-binding domains, each of which has a molecular weight of approx. 50,000. The domains differ immunologically. These domains can be liberated from the subunit by limited proteolysis.

The haemocyanin of gastropods visible under an electron microscope has a molecular weight of approx. 8 million Da and is a di-decamer. In contrast to this, the haemocyanin of cephalopods is arranged as an isolated decamer, which also differs significantly from the haemocyanin of gastropods in the quaternary structure.

The haemocyanin of the Californian keyhole limpet *Megathura crenulata* is of particular immunological interest. The haemocyanin is therefore also called keyhole limpet haemocyanin (KLH). Haemocyanins are very potent antigens. Immunization of a

vertebrate leads to a non-specific activation of the immune system which to date is not very well understood. By the general activation of the immune system, it is then possible also to achieve an immune reaction to other foreign structures which have previously been tolerated. KLH is used above all as a hapten carrier in order thus to achieve the formation of antibodies against the hapten.

In addition to *Megathura crenulata*, the abalone *Haliotis tuberculata* also belongs to the Archaegastropoda group, which is relatively old in respect of evolution. It is known that *Haliotis* also produces haemocyanin.

KLH is a mixture of two different haemocyanins, which are called KLH1 and KLH2. The subunit of KLH1 is a 390 kDa polypeptide which consists of eight globular domains called 1 a to 1 h according to their sequence in the subunit. On the other hand, KLH2 has a molecular weight of 350 kDa and according to the most recent data also contains 8 domains, called 2 a to 2 h. *In vivo* every type of subunit forms homo-oligomers, while no hetero-oligomers have been observed.

Amino-terminal, internal and carboxy-terminal domains have been obtained by limited proteolysis and crossed immunoelectrophoresis of the subunit of KLH1 and KLH2, and their amino-terminal sequences has been determined (Söhnngen et al., Eur. J. Biochem. 248 (1997), 602-614; Gebauer et al., Zoology 98(1994), 51-68). However, the resulting sequences do not allow designing of sequence-specific primers and/or probes which promise success for hybridization with genomic DNA. Although both KLH types have been known since 1991 and 1994 respectively, it has so far not been possible to clarify the primary structure.

At the DNA level, in respect of molluscs only the cDNA sequence of the haemocyanin subunit from the cephalopod *Octopus dofleini* is so far known (Miller et al., J. Mol. Biol. 278 (1998), 827-842). *Octopus dofleini* is phylogenetically very far removed from the archaegastropods. A haemocyanin gene sequence from molluscs is so far not known at all.

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),

SEQ ID NO:10 (HtH2 domain c),
 SEQ ID NO:11 (HtH2 domain d),
 SEQ ID NO:12 (HtH2 domain e),
 SEQ ID NO:13 (HtH2 domain f),
 SEQ ID NO:14 (HtH2 domain g),
 SEQ ID NO:15 (HtH2 domain h),
 SEQ ID NO:16 (partial KLH1 domain b),
 SEQ ID NO:17 (KLH1 domain c),
 SEQ ID NO:18 (KLH1 domain d),
 SEQ ID NO:19 (partial KLH1 domain e),
 SEQ ID NO:20 (KLH2 domain b),
 SEQ ID NO:21 (KLH2 domain c),
 SEQ ID NO:22 (partial KLH2 domain d),
 SEQ ID NO:23 (KLH2 domain g),
 SEQ ID NO:24 (partial KLH2 domain h),
 SEQ ID NO:49 (HtH1 domain a' + signal peptide),
 SEQ ID NO:50 (partial HtH2 domain a),
 SEQ ID NO:51 (HtH2 domain b'),
 SEQ ID NO:52 (HtH2 domain d'),
 SEQ ID NO:53 (HtH2 domain e'),
 SEQ ID NO:54 (KLH1 domain e'),
 SEQ ID NO:55 (KLH1 domain f),
 SEQ ID NO:56 (KLH1 domain g),
 SEQ ID NO:57 (KLH2 domain b'),
 SEQ ID NO:58 (KLH2 domain c'),
 SEQ ID NO:59 (KLH2 domain d'),
 SEQ ID NO:60 (KLH1 domain e),
 SEQ ID NO:61 (KLH2 domain f),
 SEQ ID NO:62 (KLH2 domain g'),
 SEQ ID NO:80 (HtH1 domain a" + signal peptide),
 SEQ ID NO:81 (HtH1 domain b"),
 SEQ ID NO:82 (HtH1 domain c"),
 SEQ ID NO:83 (HtH1 domain d"),
 SEQ ID NO:84 (HtH1 domain e"),

SEQ ID NO:85 (HtH1 domain f"),
 SEQ ID NO:86 (HtH1 domain g"),
 SEQ ID NO:87 (HtH1 domain h"),
 SEQ ID NO:88 (partial HtH2 domain a"),
 SEQ ID NO:89 (HtH2 domain b"),
 SEQ ID NO:90 (HtH2 domain c"),
 SEQ ID NO:91 (HtH2 domain d"),
 SEQ ID NO:92 (HtH2 domain e"),
 SEQ ID NO:93 (HtH2 domain f"),
 SEQ ID NO:94 (HtH2 domain g"),
 SEQ ID NO:95 (HtH2 domain h"),
 SEQ ID NO:96 (partial KLH1 domain b"),
 SEQ ID NO:97 (KLH1 domain c"),
 SEQ ID NO:98 (KLH1 domain d"),
 SEQ ID NO:99 (KLH1 domain e"),
 SEQ ID NO:100 (KLH1 domain f"),
 SEQ ID NO:101 (KLH1 domain g"),
 SEQ ID NO:102 (KLH2 domain b"),
 SEQ ID NO:103 (KLH2 domain c"),
 SEQ ID NO:104 (KLH2 domain d"),
 SEQ ID NO:105 (KLH2 domain e"),
 SEQ ID NO:106 (KLH2 domain f"),
 SEQ ID NO:107 (KLH2 domain g"),
 SEQ ID NO:108 (partial KLH2 domain h"),

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;

The "immunological properties of at least one domain of haemocyanin" means the property of a polypeptide of inducing, in the same manner as at least one domain of haemocyanin, an immunological response of the recipient immunized with the polypeptide. "Immunological response" here is understood as meaning T and/or B cell responses to haemocyanin epitopes, such as, for example, an antibody production. The immunological reaction can be observed, for example, by immunization of a mammal, such as e.g. a mouse, a rat or a rabbit, with the corresponding polypeptide and comparison of the immune response to the polypeptide used for the immunization with the immune response to natural haemocyanins.

"His tag" means a sequence of at least 6 histidine amino acids which, by corresponding cloning and fusion with an expressible sequence, leads to a fusion protein which has at least 6 His residues on the NH₂ terminus and can easily be purified by complexing with an Ni²⁺ column.

"Variants" of a nucleic acid sequences include additions, deletions, insertions or inversions and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin. Variants can be synthetic or natural. Allelic variants are an example of natural variants.

The nucleic acid sequence contained in the nucleic acid molecule according to the invention can be genomic DNA, cDNA or synthetic DNA, synthetic DNA sequences also being understood as meaning those which comprise modified internucleoside bonds. The nucleic acid sequences can furthermore be RNA sequences, which may be necessary e.g. for expression by means of recombinant vector systems. The nucleic acid sequences according to (b) are obtainable, for example, by using a detectably

marked probe which corresponds to one of the sequences described under (a) or a fragment, or a counter-strand thereof for screening cDNA/genomic DNA libraries from molluscs or arthropods. The mRNA on which the cDNA library is based is preferably to be obtained from mollusc tissues which express haemocyanin to a particularly high degree, such as e.g. mantle tissue from gastropods and branchial gland tissue from cephalopods.

Positive cDNA/genomic DNA clones are identified by standard methods. Cf. Maniatis et al., Molecular Cloning (1989) Cold Spring Harbor Laboratory Press.

In a preferred embodiment, the hybridization described under (b) or (d) is carried out under stringent conditions. Stringent hybridization conditions are e.g. 68°C overnight in 0.5 x SSC; 1% blocking reagent (Boehringer Mannheim); 0.1% sodium lauryl sarcosinate and subsequent washing with 2 x SSC; 0.1% SDS.

In a preferred embodiment, nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a) are provided. The nucleic acid sequences are preferably at least 80% homologous to one of the nucleic acid sequences described under (a). The nucleic acid sequences are particularly preferably at least 90 % homologous to one of the nucleic acid sequences described under (a). In particular, the nucleic acid sequences are at least 95% homologous to one of the nucleic acid sequences described under (a).

According to the invention, the term "homology" means homology at the DNA level, which can be determined by known methods, e.g. computer-assisted sequence comparisons (Basic local alignment search tool, S.F. Altschul et al., J. Mol. Biol. 215 (1990), 403-410).

The term "homology" known to the skilled person describes the degree to which two or more nucleic acid molecules are related, this being determined by the concordance between the sequences. The percentage of "homology" is obtained from the percentage of identical regions in two or more sequences, taking into account gaps or other sequence peculiarities.

The homology of nucleic acid molecules which are related to one another can be determined with the aid of known methods. As a rule, special computer programs with algorithms which take account of the particular requirements are employed.

Preferred methods for the determination of homology initially produce the greatest concordance between the sequences analysed. Computer programs for determination of the homology between two sequences include, but are not limited to, the GCG program package, including GAP (Devereux, J., et al., Nucleic Acids Research 12 (12): 387 (1984); Genetics Computer Group University of Wisconsin, Madison, (WI)); BLASTP, BLASTN and FASTA (Altschul, S. et al., J. Mol. Biol. 215:403-410 (1990)). The BLASTX program can be obtained from the National Centre for Biotechnology Information (NCBI) and from other sources (BLAST Handbook, Altschul S., et al., NCB NLM NIH Bethesda MD 20894; Altschul, S., et al., J. Mol. Biol. 215:403-410 (1990)). The known Smith Waterman algorithm can also be used for determining homologies.

Preferred parameters for the comparison of nucleic acid sequences include the following:

Algorithm:	Needleman and Wunsch, J. Mol. Biol 48:443-453 (1970)
Comparison matrix:	Concordance (matches) = + 10
	Non-concordance (mismatch) = 0
Gap penalty:	50
Gap length penalty:	3

The GAP program is also suitable for use with the above parameters. The above parameters are the default parameters for nucleic acid sequence comparisons.

Further algorithms, gap opening penalties, gap extension penalties and comparison matrices by way of example, including those mentioned in the Program Handbook, Wisconsin Package, version 9, September 1997, can be used. The choice depends on the comparison to be made and furthermore on whether the comparison is to be made between sequence pairs, in which case GAP or Best Fit are preferred, or between a sequence and a comprehensive sequence databank, in which case FASTA or BLAST are preferred.

A concordance of 60% determined with the abovementioned algorithm is designated 60% homology in the context of this application. The same applies accordingly to higher degrees of homology.

In a preferred embodiment, the DNA sequence according to the invention is a combination of several of the DNA sequences described under (a) to (f), which can be obtained by fusion and optionally cloning, which are known to the skilled person. These combinations are of particular interest, since they are particularly immunogenic. Combinations which contain several or all of the domains in the sequence (a to h) which occurs naturally in the subunit are particularly preferred. Embodiments in which the nucleic acid sequences which code for the domains are coupled to one another directly in frame are particularly preferred.

Constructs which comprise the nucleic acid molecules according to the invention are furthermore provided. In a preferred embodiment, the construct according to the invention comprises a promoter which is suitable for expression, the nucleic acid sequence being under the control of the promoter. The choice of promoter depends on the expression system used for expression. Generally, constitutive promoters are preferred, but inducible promoters, such as e.g. the metallothionein promoter, are also possible.

In a further preferred embodiment, the construct furthermore comprises an antigen-coding nucleic acid sequence which is bonded directly to the haemocyanin nucleic acid according to the invention. The antigen-coding sequence can be located both 5' and 3' relative to the haemocyanin sequence or also on both ends. It either follows the haemocyanin sequence directly in the same reading frame, or is coupled to it by a nucleic acid linker, the reading frame being preserved. By fusion of the antigen-coding sequence with the haemocyanin sequence the formation of a fusion protein in which the antigen-coding sequence is bonded covalently to the haemocyanin sequence is intended. The antigen according to the invention is a medically relevant antigen, which is selected, for example, from: tumour antigens, virus antigens and antigens of bacterial or parasitic pathogens. Tumour antigens can be, for example, Rb and p53. The virus antigens preferably originate from immunologically relevant viruses, such as e.g. influenza virus, hepatitis virus and HIV. Pathogen antigens are, inter alia, those from

In another preferred embodiment, the construct furthermore comprises at least a part of a vector, in particular regulatory regions, the vector being selected from: bacteriophages, such as λ derivatives, adenoviruses, vaccinia viruses, baculoviruses, SV40 viruses and retroviruses, preferably MoMuLV (Moloney murine leukaemia virus).

A construct which additionally comprises a His tag-coding DNA sequence, which, when expressed, leads to the formation of a fusion protein with a His tag on the NH₂ terminus of the haemocyanin, facilitating purification of the protein on a nickel column by chelate formation, is furthermore preferred.

The invention furthermore provides host cells which contain the construct and which are suitable for expression of the construct. Numerous prokaryotic and eukaryotic expression systems are known in the prior art, the host cells being selected, for example, from prokaryotic cells, such as *E. coli* or *B. subtilis*, from eukaryotic cells, such as yeast cells, plant cells, insect cells and mammalian cells, e.g. CHO cells, COS cells or HeLa cells, and derivatives thereof. For example certain CHO production lines of which the glycosylation patterns are altered compared with CHO cells are known in the prior art. The haemocyanins obtained using glycosylation-deficient or glycosylation-reduced host cells possibly have additional epitopes which are otherwise not accessible to the immune system of the recipient in the case of complete glycosylation, so that haemocyanins with a reduced glycosylation under certain circumstances have an increased immunogenicity. From plant cells transformed with the construct according to the invention it is possible to produce transgenic plants or plant cell cultures which produce haemocyanin polypeptides, for example tobacco, potato, tomato, sugar beet, soya bean, coffee, pea, bean, rape, cotton, rice or maize plants or plant cell cultures.

The present invention also relates to a process for the preparation of a haemocyanin polypeptide. For this, the nucleic acid molecule according to the invention and/or the

construct is expressed in a suitable host cell and the protein is isolated from the host cell or the medium by means of conventional processes.

Numerous processes for expression of DNA sequences are known to the skilled person; compare Recombinant Gene Expression Protocols in Methods in Molecular Biology, volume 62, Humana Press Totowa New Jersey (1995). The expression can be both constitutive and inducible, inducers such as, for example, IPTG and Zn^{2+} being known to the skilled person. If a His tag has been fused on to the NH_2 terminus of the haemocyanin, the haemocyanin prepared can be purified by chelate formation on a nickel column. Processes for the purification of haemocyanin, in particular KLH, are to be found in Harris et al., Micron 26 (1995), 201-212. The haemocyanin is preferably purified by ion exchange chromatography and/or gel filtration chromatography. The procedure for these measures is known to the skilled person.

In another preferred embodiment, the haemocyanin prepared according to the invention is modified. The modifications include di-, oligo- and polymerization of the monomeric starting substance, for example by crosslinking, e.g. by means of dicyclohexylcarbodiimide or pegylation or association (self assembly). The di-, oligo- and polymers prepared in this way can be separated from one another by gel filtration. The formation of decamers, didecamers or multidecamers is intended in particular. Further modifications include side chain modifications, for example of ϵ -amino-lysine residues of the haemocyanin, or amino- or carboxy-terminal modifications. Modification of the haemocyanin by covalent bonding to an antigen is particularly preferred, it being possible for the antigen to be reacted stoichiometrically or non-stoichiometrically with the haemocyanin. The antigen is preferably selected from tumour antigens, virus antigens and pathogen antigens, as mentioned above. Further modifications include post-translational events, e.g. glycosylation or partial or complete deglycosylation of the protein.

In a preferred embodiment, the haemocyanin obtained by recombinant expression in prokaryotes or glycosylation-deficient eukaryotes is non-glycosylated. Haemocyanin which is glycosylated by recombinant expression in eukaryotes which are capable of glycosylation, such as yeast cells, plant cells, insect cells or mammalian cells, such as CHO cells or HeLa cells, is also possible according to the invention.

Haemocyanin polypeptides which comprise an amino acid sequence, the amino acid sequence being coded by one or more of the nucleic acid molecules according to the invention, are provided in another embodiment,

Haemocyanin polypeptides which comprise at least one amino acid sequence selected from the following group:

SEQ ID NO:25 (HtH1 domain a + signal peptide),
 SEQ ID NO:26 (HtH1 domain b),
 SEQ ID NO:27 (HtH1 domain c),
 SEQ ID NO:28 (HtH1 domain d),
 SEQ ID NO:29 (HtH1 domain e),
 SEQ ID NO:30 (HtH1 domain f),
 SEQ ID NO:31 (HtH1 domain g),
 SEQ ID NO:32 (HtH1 domain h),
 SEQ ID NO:33 (partial HtH2 domain b),
 SEQ ID NO:34 (HtH2 domain c),
 SEQ ID NO:35 (HtH2 domain d),
 SEQ ID NO:36 (HtH2 domain e),
 SEQ ID NO:37 (HtH2 domain f),
 SEQ ID NO:38 (HtH2 domain g),
 SEQ ID NO:39 (HtH2 domain h),
 SEQ ID NO:40 (partial KLH1 domain b),
 SEQ ID NO:41 (KLH1 domain c),
 SEQ ID NO:42 (partial KLH1 domain d),
 SEQ ID NO:43 (partial KLH1 domain e),
 SEQ ID NO:44 (KLH2 domain b),
 SEQ ID NO:45 (KLH2 domain c),
 SEQ ID NO:46 (partial KLH2 domain d),
 SEQ ID NO:47 (KLH2 domain g),
 SEQ ID NO:48 (partial KLH2 domain h),
 SEQ ID NO:63 (HtH1 domain a' + signal peptide),
 SEQ ID NO:64 (HtH1 domain h'),

"homology" is obtained from the percentage of regions in concordance in two or more sequences, taking into account gaps or other sequence peculiarities.

The expression "conservative amino acid exchange" relates to an exchange of an amino acid residue for another amino acid residue, where the exchange does not lead to a change in polarity or charge. An example of a conservative amino acid exchange is the exchange of a non-polar amino acid residue for another non-polar amino acid residue.

The homology of polypeptide molecules which are related to one another can be determined with the aid of known methods. As a rule, special computer programs with algorithms which take account of the particular requirements are employed. Preferred methods for the determination of homology initially produce the greatest concordance between the sequences analysed. Computer programs for determination of the homology between two sequences include, but are not limited to, the GCG program package, including GAP (Devereux, J., et al., *Nucleic Acids Research* 12 (12): 387 (1984); Genetics Computer Group University of Wisconsin, Madison, (WI)); BLASTP, BLASTN and FASTA (Altschul, S. et al., *J. Molec. Biol* 215:403/410 (1990)). The BLAST X program can be obtained from the National Centre for Biotechnology Information (NCBI) and from other sources (BLAST Handbook, Altschul S., et al., NCB NLM NIH Bethesda MD 20894; Altschul, S., et al., *J. Mol.* 215:403/410 (1990)). The known Smith Waterman algorithm can also be used for determining homology.

Preferred parameters for the sequence comparison include the following:

Algorithm:	Needleman and Wunsch, <i>J. Mol. Biol</i> 48:443-453 (1970)
Comparison matrix:	BLOSUM 62 of Henikoff and Henikoff, <i>Proc. Natl. Acad. Sci. USA</i> 89:10915-10919 (1992)
Gap penalty:	12
Gap length penalty:	4
Similarity threshold:	0

The GAP program is also suitable for use with the above parameters. The above parameters are the standard parameters (default parameters) for amino acid sequence comparisons where gaps at the ends do not reduce the homology value. If sequences are very short

Further algorithms, gap opening penalties, gap extension penalties and comparison matrices by way of example, including those mentioned in the Programm-Handbuch, Wisconsin-Paket [Program Handbook, Wisconsin Package], version 9, September 1997, can be used. The choice depends on the comparison to be made and furthermore on whether the comparison is to be made between sequence pairs, in which case GAP or best fit are preferred, or between a sequence and a comprehensive sequence database, in which case FASTA or BLAST are preferred.

In another embodiment, the invention provides haemocyanin polypeptides which are obtainable by the recombinant preparation method or modifications thereof.

Haemocyanin 1 from *Haliotis tuberculata*, which has an apparent molecular weight of 370 kDa in SDS-PAGE under reducing conditions, is particularly preferred.

Haemocyanin 2 from *Haliotis tuberculata*, which has an apparent molecular weight of 370 kDa in SDS-PAGE under reducing conditions, is furthermore particularly preferred.

The haemocyanins are obtainable from whole haemocyanin from *Haliotis tuberculata* by the selective dissociation process described in the examples.

In particular, the invention provides the use of a nucleic acid molecule according to the invention which is bonded to an antigen-coding DNA sequence for specific immunization against this antigen. Without being bound to this theory, the immunization here is based on non-specific stimulation of the immune system by haemocyanin polypeptide epitopes and more extensive specific immunization by recognition of antigen epitopes by the immune system.

Such an immunization is particularly valuable in respect of pathogen antigens, and especially in respect of tumour antigens. The usability of the pharmaceutical composition according to the invention for treatment of tumour diseases also results from the cross-reactivity of the haemocyanin-specific antibodies with carbohydrate residues, which occur on the surface of tumours, such as e.g. the Thomsen-Friedenreich antigen, which occurs in the majority of human tumours, such as epithelial carcinomas, ovarian carcinoma, colorectal carcinoma, mammary carcinoma, bronchial carcinoma and bladder carcinoma.

The pharmaceutical compositions according to the invention can furthermore be employed for treatment of parasitic diseases, such as schistosomiasis, and for prevention of cocaine abuse.

Pharmaceutical compositions which comprise a haemocyanin polypeptide according to the invention in combination with one or more physiologically tolerated additives are provided as a further embodiment of the present invention. As already mentioned above, such a haemocyanin polypeptide can consist of a complete haemocyanin subunit, of one or more domains and of one or more fragments of such domains, provided that these fragments still have the immunological properties of at least one domain of a haemocyanin. Such a pharmaceutical composition is suitable e.g. as an antiparasitic composition, antiviral composition or antitumour composition due to either the non-specific immunostimulation, which is to be attributed solely to the haemocyanin, or due to the specific immune reaction to antigens associated with the haemocyanin. It can thus be employed e.g. for treatment of schistosomiasis, epithelial carcinomas, ovarian carcinoma, colorectal carcinoma, mammary carcinoma, bronchial carcinoma and bladder carcinomas, but is also suitable for treatment of high blood pressure. The treatment of high blood pressure is achieved by carrying out an immunization with the aid of haemocyanin- β -adrenergic receptor peptide constructs and/or fusion proteins.

In another embodiment, the pharmaceutical compositions according to the invention are used as vaccines. They can thus make a valuable contribution to the prophylaxis of diseases caused by known pathogens. This applies in particular to pharmaceutical compositions in which a haemocyanin polypeptide is coupled to a virus, virus

According to another preferred embodiment, the pharmaceutical composition according to the invention is used for prevention of cocaine abuse.

Various methods for the preparation of liposomes which can be used for pharmaceutical purposes are known to the skilled person. The selectivity of the liposomes comprising the nucleic acid molecules or haemocyanin polypeptides according to the invention can be increased by the additional incorporation into the liposome of cell recognition molecules, which bind selectively to target cells. Receptor ligands which bind to receptors of the target cells or, especially in the case of tumours, antibodies directed against surface antigens of the particular target cells envisaged are particularly suitable for this.

The vaccines are formulated by methods known to the skilled person; in some embodiments the additional use of adjuvants, such as e.g. Freund's adjuvant or polysaccharides, is envisaged.

The invention furthermore provides antibodies which react specifically with the haemocyanin polypeptide according to the invention and are obtainable by immunization of a test animal with a haemocyanin polypeptide. Polyclonal antibodies can be obtained

- (a) Electron microscopy of negatively stained whole HtH, which has been purified by ultracentrifugation of cell-free haemolymph;
- (b) SDS polyacrylamide gel electrophoresis (7.5% polyacrylamide) of HtH1 compared with KLH (MW 370 kDa);
- (c) Native polyacrylamide gel electrophoresis (5% polyacrylamide) of the HtH subunit preparation, the anode being at the lower edge;
- (d) Crossed immunoelectrophoresis of the two HtH subunits using anti-HtH antibodies from the rabbit;
- (e) Electron microscopy of the remaining HtH1 didecamers (white arrows) after selective dissociation of HtH2 (black arrows);

- (f) Elution profile of the gel filtration chromatography (Biogel A15m) in the presence of ammonium molybdate/polyethylene glycol solution (pH 5.9) after selective dissociation of HtH2 into its subunit and subsequent concentration of HtH1 by ultracentrifugation;
- (g) Native polyacrylamide gel electrophoresis (6.5% polyacrylamide) of HtH1 and HtH2 subunits purified by gel chromatography compared with the starting material;
- (h,i) Crossed immunoelectrophoresis of chromatographically purified HtH subunits; and
- (j,m) Crossed immunoelectrophoresis of the purified HtH subunits using anti-KLH antibodies from the rabbit which are specific for KLH1 and KLH2.

Fig. 2 shows the analysis of the subunit organization of HtH1, anti-HtH1 antibodies from the rabbit having been used for the immunoelectrophoresis and the anode being on the left-hand side;

- (a) Crossed immunoelectrophoresis after limited proteolysis of HtH1 with the aid of elastase;
- (b) SDS polyacrylamide gel electrophoresis (7.5% polyacrylamide) of the elastase-cleaved HtH1 subunit;
- (c,d,g-j,l,n,p) Crossed immunoelectrophoresis of the elastase cleavage products of the HtH1 subunit;
- (e) Crossed immunoelectrophoresis after limited proteolysis of HtH1 with the aid of V8 protease;
- (f) SDS polyacrylamide gel electrophoresis (7.5% polyacrylamide) of the V8 protease-cleaved HtH1 subunit;
- (k,m,o) Crossed immunoelectrophoresis after limited proteolysis of HtH1 with the aid of the three stated proteases.

Fig. 3 shows the separation of proteolytic cleavage products of the subunit HtH1 with the aid of HPLC.

Fig. 4 shows the cDNA sequence of HtH1 in combination with the intron structure.

Fig. 5 shows the primary structure deduced for HtH1.

Fig. 6 shows the cDNA sequence of Hth2 in combination with the intron structure.

Fig. 7 shows the primary structure deduced for Hth2.

Fig. 8 shows the cDNA sequence of KLH1 in combination with the intron structure.

Fig. 9 shows the primary structure deduced for KLH1.

Fig. 10 shows the cDNA sequence of KLH2 in combination with the intron structure.

Fig. 11 shows the primary structure deduced for KLH2.

EXAMPLES

Material and methods

1. Preparation of the haemolymph and isolation of haemocyanin

Individuals of the European abalone *Haliotis tuberculata* from the French Atlantic coast region were provided by S.M.E.L (Blainville sur Mer, France) and Biosyn (Fellbach, Germany). The animals were kept in a 300 l sea-water aquarium at 17°C and fed with brown algae. For removal of the haemolymph, the abalones were placed on ice in a closed plastic bag. After one hour, large volumes of haemolymph had been secreted through their skin. It emerged that the haemocyanin obtained by this process is identical to the haemocyanin which could be collected by cutting a hollow in the foot of cooled-down sea snails using a scalpel blade. The blood cells were separated from the haemolymph by centrifugation at 800 g for 30 min at 4°C. The whole haemocyanin was then immediately sedimented by preparative ultracentrifugation at 30,000 g for 4 hours at 4°C. The supernatant was discarded and the blue haemocyanin pellet was suspended overnight in "stabilization buffer" (0.05 M Tris, 5 mM CaCl₂, 5 mM MgCl₂, 0.15 M NaCl, 1 mM PMSF, pH 7.4) and stored at 4°C.

Using the process described by Harris et al., 1995, supra, intact Hth1 was obtained from the whole Hth by selective dissociation of Hth2 in ammonium molybdate/polyethylene

glycol (1%/0.2%) solution, pH 5.9 and subsequent ultracentrifugation. The partly purified HtH1 pellet formed was dissolved and purified to homogeneity by gel filtration on a Biogel A15m device. The last step resulted in small amounts of purified HtH2. Native HtH1 and HtH2 was dissociated quantitatively into the subunits by dialysis against "dissociation buffer" (0.13 M glycine/NaOH, pH 9.6) at 4°C overnight; the presence of EDTA was not necessary. 1 mM PMSF was added at each stage of the purification to inhibit proteolysis.

2. Electron microscopy

Conventional "negative staining" was carried out by the individual drop method (Harris and Horne in Harris, J.R. (editors) *Electron microscopy in biology*, (1991), IRL Press Oxford, p. 203-228). Carbon carrier films were initially subjected to glow discharge for 20 seconds to render them hydrophilic and adsorptive for the protein. The protein samples are allowed to adsorb on to the carbon films for 60 seconds. The buffer salts are then removed by sequential washing with four successive 20 µl drops of water. Finally, the gratings are negatively stained with a 20 µl drop of 5% aqueous ammonium molybdate containing 1% trehalose (pH 7.0) and left to dry at room temperature. A Zeiss EM 900 transmission electron microscope is used for the electron microscopy analysis.

3. Polyacrylamide gel electrophoresis and immunoelectrophoresis

SDS polyacrylamide gel electrophoresis (SDS-PAGE) was carried out by the method of Laemmli (*Nature* 227 (1970), 670-685). An alkaline system according to Markl et al. (1979) *J. Comp. Physiol.* 133 B, 167-175 with a 0.33 M Tris/borate, pH 9.6 as the gel buffer and 0.065 M Tris/borate, pH 9.6 as the electrode buffer was used for the native PAGE. Crossed and "crossed-line" immunoelectrophoresis (IE) were carried out in accordance with Weeke (*Scand. J. Immunol.* 2 (1973), Suppl. 1, 47-56) or Kroll (*Scand. J. Immunol.* 2, Suppl. 1 (1973), 79-81). Rabbit antibodies against dissociated whole HtH and purified HtH1 were produced by Charles River Deutschland (Kisslegg, Germany). The immunization process was carried out in accordance with Markl and Winter (*J. Comp. Physiol.* 159B (1989), 139-151).

4. Limited proteolysis and isolation of the fragments

The limited proteolysis was carried out at 37°C in 0.13 M glycine/NaOH, pH 9.6 by addition of one of the following enzymes (Sigma, Deisenhofen, Germany), which were dissolved in 0.1 M NH_4HCO_3 , pH 8.0: *Staphylococcus aureus* V8 protease type XVII (8400), papain type II from papaya milk (P-3125), bovine pancreas elastase type IV (E-0258), chymotrypsin and trypsin. The haemocyanin concentration was between 1 and 10 mg/ml. The final concentration of the enzyme was 2% (weight/weight). The proteolysis was ended after 5 hours by freezing to -20°C. The HPLC process was carried out on a device from Applied Biosystems (BAI, Bensheim, Germany) equipped with a model 1000S Diode Array detector. The proteolytic fragments were introduced on to a small Mono-Q anion exchanger column (Pharmacia, Freiburg, Germany), which had been equilibrated with 0.02 M Tris/HCl, pH 8.0, and were eluted with a linear sodium chloride gradient (0.0 M – 0.5 M CaCl) in the same buffer at a flow rate of 1 ml/min. Alternatively, the proteolytic fragments were isolated by cutting out the bands from native PAGE gels (Markl et al., 1979) J. Comp. Physiol. **133** B, 167-175, after they had first been inversely stained with the Roti-White system (Roth, Karlsruhe, Germany) in accordance with Fernandez-Patron et al. (1995) Anal. Biochem. **224**, 203-211. For subsequent cleavage with a second enzyme, the fragments isolated were first dialysed overnight against 0.13 M glycine/NaOH, pH 9.6 to remove NaCl.

5. Amino acid sequence analysis

The proteins obtained by the HPLC process were denatured in SDS-containing sample buffer and separated by SDS-PAGE (Laemmli, 1970, supra; 7.5 % polyacrylamide). To prevent blocking of the NH_2 terminus, 0.6% (weight/weight) thioglycolic acid was added to the cathode buffer (Walsh et al., Biochemistry **27** (1988), 6867-6876). The protein bands were transferred by electro-transfer to ProBlot membranes (Applied Biosystems, Germany) in a vertical blotting chamber (25 mM borate buffer, pH 8.8, containing 2 mM EDTA; 10 min/100 mA, 15 min/200 mA, 12 h/300 mA). Detection of the individual polypeptides on the membranes was carried out with Ponceau S stain. The polypeptide bands of interest were cut out and sequenced in a 477A protein sequencing device from Applied Biosystems. The amounts of polypeptides applied to the sequencing device were in the lower pmol range.

6. cDNA cloning and sequence analysis

A lambda-cDNA expression library was established from poly(A⁺)-RNA from *Haliotis* mantle tissue using the vector Lambda ZAP Express[®] in accordance with the manufacturer's instructions (Stratagene, Heidelberg, Germany). The clones were isolated using HtH-specific rabbit antibodies. The nucleotide sequencing was carried out on both strands using the Taq Dye deoxy Terminator[®] system. The sequences were arranged with the software CLUSTAL W (1.7)[®] and TREEVIEW[®] (Thompson et al., Nucl. Acids Res. 22 (1994), 4673-4680).

Example 1:

Isolation of HtH and separation of two different types (HtH1 and HtH2)

The haemolymph was obtained from adult abalones. The blood cells were removed by centrifugation and the haemocyanin was then sedimented by ultracentrifugation. The blue haemocyanin pellet was dissolved again in "stabilization buffer" (pH 7.4) and examined by electron microscopy (figure 1a). It comprised mainly typical di-decamers, accompanied by a small content of decamers and tridecamers. Denaturing in 2% SDS in the presence of reducing substances and subsequent SDS-PAGE separation resulted in a single band, which corresponded to the polypeptide with an apparent molecular weight of 370 kDa, which is only slightly below the apparent subunit weight of KLH (figure 1b). Complete dissociation of the oligomers and of the di-decamers into the native polypeptides (subunits) was achieved by overnight dialysis of HtH against "dissociation buffer" (pH 9.6). The native PAGE method, which was used on these samples, showed a main and a secondary component (figure 1c). Crossed immunoelectrophoresis (crossed IE) using polyclonal rabbit antibodies generated against purified whole HtH showed two components which are immunologically different but show the classical reaction of being partly immunologically identical (figure 1d). Their preparative isolation (figure 1e-i) showed that they are subunits of two different HtH types, called HtH1 and HtH2, and the patterns of the native PAGE and crossed IE methods could be assigned to each individually (figure 1c, d).

The separation of HtH1 and HtH2 was carried out by the method of selective dissociation according to Harris et al., 1995, *supra*. In ammonium molybdate/polyethylene glycol, HtH1 in the oligomer state (di-decamer) was completely stable, while HtH2 dissociated completely into the subunits (figure 1e). This allowed quantitative sedimentation of HtH1 in an ultracentrifuge, while the majority of the HtH2 remained in the supernatant. Large amounts of HtH1 were purified to homogeneity from the redissolved pellet by gel filtration chromatography, which also resulted in small amounts of pure HtH2 (figure 1f). The fractions were investigated by native PAGE (figure 1g) and crossed IE (figure 1h, i). The process of selective dissociation of HtH2 removed all the tri-decamer from the samples, which suggests that the latter are built up from HtH2, but not from HtH1 (figure 1e). The selective dissociation behaviour of HtH2 and also the ability to form aggregates which are larger than *in vivo* di-decamers correspond to the properties of KLH2. Conversely, the stability of HtH1 under these conditions and its inability to assemble into aggregates larger than di-decamers resemble the behaviour of KLH1. This feature of being related is demonstrated further by the reaction of anti-KLH1 and anti-KLH2 antibodies against the two HtH types (figure 1j-m).

Example 2:

Analysis of the organization of the HtH1 subunit

The eight functional units (FUs, often called "functional domains") which form a mollusc haemocyanin subunit differ in primary structure and show no immunological cross-reactivity, as emerged from crossed IE. In the case of the purified HtH1 subunit (Figure 1g, h), small concentrations of five different proteases (elastase, V8 protease, papain, trypsin and chymotrypsin) which had cleaved the peptide bonds between adjacent FUs of KLH1 and KLH2 were used (Gebauer et al., 1994, *supra*, Söhnngen et al., 1997, *supra*). The cleavage products were investigated by crossed IE and SDS-PAGE (Fig. 2). Elastase treatment produces eight individual FUs, deduced from the number of different immunoprecipitation peaks in the crossed IE (Fig. 2a) and with the apparent molecular weight of approx. 50 kDa of the main portion of the cleavage products in SDS-PAGE (Fig. 2b). A further precipitation peak was recognized as FU dimer, which was formed by incomplete cleavage of the segment ab (Fig. 2a). By an HPLC process with a Mono-Q column (Fig. 3a), two of the elastase cleavage products

were obtained in a sufficient purity to allow their clear assignment to two of the eight precipitation peaks (Fig. 2c, d) by "crossed-line IE". The other four proteases had different cleavage patterns, which comprised mixtures of individual FUs and larger fragments containing two, three or more FUs (e.g. Fig. 2e, f). Many of them were concentrated to a sufficient amount by the HPLC process (Fig. 3b-e) to allow their identification in their corresponding SDS-PAGE and crossed IE patterns. A number of these components were sequenced N-terminally by blot transfer of SDS gels on ProBlot® membranes (Table 1). The results were compared with the N-terminal sequences which had been obtained from the apparently orthologous protein in *Megathura crenulata*, KLH1 (Table I), the complete FU arrangement of which is available (Söhngen et al., 1997, supra; cf. Fig. 5b). The result of the entire batch led to the determination of the complete FU arrangement within the HtH1 subunit (Fig. 2a).

In particular, cleavage of the HtH1 subunit (1-abcdefgh) with V8 protease resulted in four precipitation peaks in the crossed IE (Fig. 2e). The SDS-PAGE showed five different fragments (Fig. 2f): 220 kDa (5 FUs), 185 kDa (4 FUs), 100 kDa (2 FUs), 55 kDa (1 FU) and 46 kDa (1 FU). The 100 kDa fragment was isolated by the HPLC method (Fig. 3b) and identified by N-terminal sequencing as 1-ab, since the sequence was identical to that of the intact subunit (Table I). In the "crossed-line" IE process, 1-ab fused with three precipitation peaks of the elastase cleavage pattern. On the basis of the evaluation, they represent fragments 1-ab, 1-a and 1-b (Fig. 2g). However, it remained unclear which peak represents 1-a and which 1-b. In a second step, the 1-ab purified by HPLC was cleaved by elastase into its component FUs, from which one could be eluted by the native PAGE gel strip method and was assigned to the elastase pattern by the "crossed-line" IE method (Fig. 2h) and sequenced N-terminally. This component had the same N-terminal sequence as the whole subunit and was therefore identical to 1-a. The second FU of the 100 kDa fragment is thus 1-b (Fig. 2a; Table I). HPLC-purified 1-c and 1-h were also obtained (Fig. 3b), identified by N-terminal sequence similarities with the corresponding FUs in KLH1 (Table I) and assigned by the "crossed-line" IE method to their corresponding precipitation peaks in the elastase pattern (Fig. 2i, j). 1-a, 1-b, 1-c and 1-h were furthermore identified (Fig. 2a). Using papain for subunit cleavage, five different peaks were obtained in the crossed IE method (Fig. 2k). A 100 kDa fragment (2 FUs) was purified from such a sample by the HPLC method (Fig. 3c), and, according to the "crossed-line" IE method, contained the FU 1-h already identified and one of the four

FUs still not identified and therefore must be 1-gh (Fig. 2k, 3c). In fact, this fragment had an N-terminal sequence which showed similarities with KLH1-g (Table I). For further confirmation, the HPLC-purified fragment 1-gh was cleaved into its constituent FUs with elastase, from which 1-g was purified and identified by N-terminal sequencing. It was assigned to its peak in the elastase cleavage pattern by the "crossed-line" IE method (Fig. 2l).

The 220 kDa fragment from the V8 protease cleavage (Fig. 2e, f) was purified by HPLC (Fig. 3b) and in the "crossed-line" IE method fused with 1-h, 1-g and three peaks of the elastase cleavage pattern which have not yet been identified. The 185 kDa fragment was furthermore obtained in a sufficient purity (Fig. 2e, f; 3b), and it was shown that it comprised the same components with the exception of 1-h. This suggested that the 22 kDa and the 185 kDa fragment are 1-defgh and 1-defg respectively. In fact, the N-terminal sequence was practically identical and furthermore showed similarity with KLH1-d (Table I). Cleavage of the HtH1 subunit with trypsin resulted in a large number of components in the molecular weight range of one or two FUs (Fig. 2m). Several of the components were concentrated in HPLC fractions (Fig. 3d). A 100 kDa fragment proved to be particularly useful since it had the same N-terminal sequence as the fragment 1-defg from the v8 protease cleavage (Table I); the 100 kDa fragment should therefore be 1-de. In the "crossed-line" IE method, this component fused with two of the three FU peaks of the elastase cleavage pattern not yet identified (Fig. 2n), which should therefore be 1-d and 1-e, and thus left a single possibility for 1-f. The "crossed-line" IE method also showed that FU 1-f was furthermore present in the 1-de fraction (Fig. 2n). The identification of 1-f was confirmed by cleavage of the subunit with chymotrypsin (Fig. 2o) and a subsequent HPLC process (Fig. 3e). This cleavage gave, inter alia, a 95 kDa fragment (2 FUs) which fused with 1-g and a second peak (Fig. 2p) in the "crossed-line" IE method and could therefore be either 1-gh (which could be ruled out since 1-h had already been identified) or 1-fg (which seems appropriate on the basis of the further peak in question, which was identical to the remaining candidate). In fact, this fragment showed a new N-terminal sequence which is similar to KLH1-f in a certain manner. The last problem was now to assign the two remaining FU peaks to 1-d and 1-e. This was achieved using HPLC-isolated FUs from samples in which the subunit had been cleaved with elastase. (Fig. 2c, d; 3a). The more acidic component in the crossed IE method was deduced as 1-d from its N-terminal sequence, which is identical to that of 1-defgh (Fig.

2c, Table I), while the more basic component of the 1-d/1-g pair had a new N-terminal sequence (Table I) and therefore had to be 1-e (Fig. 2a). The structure of the functional units of subunit HtH1 was thus clarified.

Example 3:

Comparison of the molecular weights and N-terminal sequences of the biochemically isolated functional units (FUs) from HtH1 and KLH1. The various FUs, each with an intact binuclear copper-binding site, were liberated from their larger unit as globular segments by limited proteolysis; cf. the section "Isolation and analysis of the units from HtH1". The KLH1 data were obtained from Söhnngen et al., *supra*. The assignment as an actual unit was done on the basis of the molecular weight and the immunological properties (cf. Fig. 2). The unusually low molecular weight of isolated HtH1-d could mean that a large peptide was split off C-terminally.

TABLE 1

Functional unit	Weight (kDa)	N-terminal sequence
HtH1-a	53	DNV VRK DVSHLTDDDEVQ
KLH1-a	50	ENL VRK DVERL
HtH1-b	48	?
KLH1-b	45	?
HtH1-c	46	FEDEKHSLR IRK NVDSLTPPEENTNERLR
KLH1-c	45	KVPRSRL IRK NVDRLTPSE
HtH1-d	40	VEEVTGASH IRK NLNDLNTGEM
KLH1-d	50	EVTSANR IRK NIENLS
HtH1-e	49	ILDHDHEEEIL VRK NIIDLSP
KLH1-e	50	?
HtH1-f	50	KLNSRKHTPNR VRH ELSSLSSRDIASLKA
KLH1-f	45	HHLSXNK VRH DLSTL
HtH1-g	45	DHQSGSIAGSG VRK DVNTLTKAETDNLRE
KLH1-g	45	SSMAGHF VRK DINTLTP
HtH1-h	55	DEHHDDLADVL IRK EVDFLSLQEANAIDK
KLH1-h	60	HEDHHEDIL VRK NIHSL

Example 4:

Cloning of haemocyanin cDNA

1. For cloning the cDNA of haemocyanin, mRNA was isolated from the mantle tissue of the particular mollusc. The first cDNA strand was obtained by reverse transcription with Oligo(dT) as a primer. The second strand was obtained conventional synthesis with random primers. The cDNA obtained in this way was cloned in a lambda expression vector to form a cDNA expression library. Using an anti-haemocyanin antibody, the library was searched under suitable conditions, positive clones being obtained. These positive clones were isolated, sequenced and characterized.

2. A cDNA probe was prepared from the N-terminal region of a positive clone obtained, and the cDNA library was searched with this. The positive clones obtained were in turn isolated, sequenced and characterized.
3. To obtain sequences arranged still further to 5', another expression library was established from cDNA, this being obtained with the aid of a combination of haemocyanin-specific and "random" primers. This cDNA library was searched with cDNA probes which correspond to the "N-terminal" regions of the positive clones obtained under (2.). The positive clones obtained were isolated, sequenced and characterized.

Example 5:

Cloning of haemocyanin genes

Genomic DNA was isolated by standard methods. The PCR reaction was carried out with the aid of haemocyanin-specific primers in order to amplify the gene sections of the haemocyanins of interest. The amplification products obtained were cloned in a suitable vector (for example pGem T or pGem T easy (Promega, Mannheim) sequenced and characterized.

Example 6:

Recombinant expression of haemocyanin

A PCR reaction was carried out with a cDNA clone which contains the coding sequence for HtH-1d in order to amplify specifically the coding sequence of the domain 1d.

Synthetically prepared oligonucleotides were used as primers.

Primer 1 (upstream) comprises six nucleotides of the end of the domain HtH-1c, an *SacI* cleavage site and 12 nucleotides of the end of the domain HtH-1d.

Primer 2 (downstream) comprises six nucleotides of the start of the domain HtH-1e, an *SaII* cleavage site and an HtH1-d-specific sequence.

PCR conditions:	2	min	95°C
	30	sec	95°C
	30	sec	55°C
	1	min	72°C
	35	cycles	
	10	min	72°C

The amplification product was cloned in the pGEM T easy PCR cloning vector (Promega) in XL-1 Blue (Stratagene). After isolation of the recombinant plasmid and restriction with *SacI* and *SalI*, the cDNA of domain 1d could be isolated. The expression vector pQE30 (Qiagen) was also restricted with the corresponding enzymes.

The ligation was then carried out between the Hth-1d-cDNA (restricted with *SacI* and *SalI*) and pQE (restricted with *SacI* and *SalI*). Directed cloning of the cDNA which codes for Hth-1d in an expression vector is thus possible. The expression of Hth1-d in pQE in XL-1 Blue is carried out in accordance with the manufacturer's instructions. The expression of further Hth1, Hth2 or KLH1 or KLH2 domains can be carried out analogously.

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WHAT IS CLAIMED IS:

1. Nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(a) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),

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SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),
SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),

(b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;

(c) nucleic acid sequences which on the basis of the genetic code are degenerate to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;

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4. Nucleic acid molecule according to claim 1, **characterized in that** the nucleic acid molecule described under (e) is at least 90 % homologous to one of the nucleic acid sequences described under (a).

5. Nucleic acid molecule according to claim 1, **characterized in that** the nucleic acid molecule described under (e) is at least 95 % homologous to one of the nucleic acid sequences described under (a).

6. Nucleic acid molecule according to claim 1,
characterized in that it is a deoxyribonucleic acid
molecule.

7. Construct comprising a nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(a) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),

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SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),

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SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),
SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
SEQ ID NO:103 (KLH2 domain c"),
SEQ ID NO:104 (KLH2 domain d"),
SEQ ID NO:105 (KLH2 domain e"),

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SEQ ID NO:106 (KLH2 domain f"),

SEQ ID NO:107 (KLH2 domain g"),

SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin;

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and

(g) combinations of several of the DNA sequences described under (a) to (f)

8. Construct according to claim 7, further comprising a promoter which is suitable for expression control, the nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof being under the control of the promoter.

9. Construct according to claim 7, further comprising a nucleic acid sequence which codes for an antigen and is coupled directly to the nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof.

10. Construct according to claim 9, wherein the antigen is selected from: tumour antigens, virus antigens and antigens of bacterial or parasitic pathogens.

11. Construct according to claim 7, wherein the construct comprises at least a part of a vector, the vector being selected from: bacteriophages, adenoviruses, vaccinia viruses, baculoviruses, SV40 virus and retroviruses.

12. Construct according to claim 7, wherein the

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SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
SEQ ID NO:103 (KLH2 domain c"),
SEQ ID NO:104 (KLH2 domain d"),
SEQ ID NO:105 (KLH2 domain e"),
SEQ ID NO:106 (KLH2 domain f"),
SEQ ID NO:107 (KLH2 domain g"),
SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;

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- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and
- (g) combinations of several of the DNA sequences described under (a) to (f).

14. Host cell according to claim 13, **characterized in that** the prokaryotic host cell is selected from E. coli and Bacillus subtilis.

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15. Host cell according to claim 13, **characterized in that** the eukaryotic host cell is selected from yeast cells, plant cells, insect cells and mammalian cells, preferably from CHO cells, COS cells and HeLa cells.

16. Process for the preparation of a haemocyanin polypeptide, wherein a nucleic acid molecule and/or a construct comprising said nucleic acid molecule is expressed in a suitable host cell and the protein is isolated, if appropriate, wherein said nucleic acid molecule comprising a nucleic acid molecule comprises a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(a) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),

SEO ID NO:2 (HtH1 domain b),

SEQ ID NO:3 (HtH1 domain c),

SEQ ID NO:4 (HtH1 domain d),

SEQ ID NO:5 (HtH1 domain e),

SEQ ID NO:6 (HtH1 domain f),

SEQ ID NO:7 (HtH1 domain q),

SEQ ID NO: 8 (HtH1 domain h),

SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),

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SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
SEQ ID NO:103 (KLH2 domain c"),
SEQ ID NO:104 (KLH2 domain d"),
SEQ ID NO:105 (KLH2 domain e"),
SEQ ID NO:106 (KLH2 domain f"),
SEQ ID NO:107 (KLH2 domain g"),
SEQ ID NO:108 (partial KLH2 domain h");

(b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence

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according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;

- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin;
and
- (g) combinations of several of the DNA sequences described under (a) to (f).

17. Process according to claim 16, **characterized in**

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that the haemocyanin polypeptide prepared is modified naturally or chemically.

18. Process according to claim 17, **characterized in that** the modification is a crosslinking or a covalent bonding to an antigen.

19. Process according to claim 16, **characterized in that** the expression is carried out in a host cell.

20. Haemocyanin polypeptide, comprising an amino acid sequence which is coded by one or more of a nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(a) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),

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SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),

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SEQ ID NO:80 (HtH1 domain a" + signal peptide),
SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
SEQ ID NO:103 (KLH2 domain c"),
SEQ ID NO:104 (KLH2 domain d"),
SEQ ID NO:105 (KLH2 domain e"),
SEQ ID NO:106 (KLH2 domain f"),
SEQ ID NO:107 (KLH2 domain g"),
SEQ ID NO:108 (partial KLH2 domain h");

(b) nucleic acid sequences which hybridize with the

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counter-strand of a nucleic acid sequence
according to (a) and code for a polypeptide which
has the immunological properties of at least one
domain of a haemocyanin;

(c) nucleic acid sequences which on the basis of the
genetic code are degenerated to the DNA sequences
defined under (a) and (b) and code for a
polypeptide which has the immunological properties
of at least one domain of a haemocyanin;

(d) nucleic acid sequences which hybridize with one
of the nucleic acid sequences described under (a)
to (c) and the counter-strand of which codes for a
polypeptide which has the immunological properties
of at least one domain of a haemocyanin;

(e) nucleic acid sequences which are at least 60%
homologous to one of the nucleic acid sequences
described under (a);

(f) variants of the sequences described under (a) to
(d), the variants containing additions, deletions,
insertions or inversions with respect to the
sequences described under (a) to (d) and coding
for a polypeptide which has the immunological
properties of at least one domain of haemocyanin;
and

(g) combinations of several of the DNA sequences
described under (a) to (f).

SEQ ID NO:25 (HtH1 domain a + signal peptide),
SEQ ID NO:26 (HtH1 domain b),
SEQ ID NO:27 (HtH1 domain c),
SEQ ID NO:28 (HtH1 domain d),
SEQ ID NO:29 (HtH1 domain e),
SEQ ID NO:30 (HtH1 domain f),
SEQ ID NO:31 (HtH1 domain g),
SEQ ID NO:32 (HtH1 domain h),
SEQ ID NO:33 (partial HtH2 domain b),
SEQ ID NO:34 (HtH2 domain c),
SEQ ID NO:35 (HtH2 domain d),
SEQ ID NO:36 (HtH2 domain e),
SEQ ID NO:37 (HtH2 domain f),
SEQ ID NO:38 (HtH2 domain g),
SEQ ID NO:39 (HtH2 domain h),
SEQ ID NO:40 (partial KLH1 domain b),
SEQ ID NO:41 (KLH1 domain c),
SEQ ID NO:42 (partial KLH1 domain d),
SEQ ID NO:43 (partial KLH1 domain e),
SEQ ID NO:44 (KLH2 domain b),
SEQ ID NO:45 (KLH2 domain c),
SEQ ID NO:46 (partial KLH2 domain d),
SEQ ID NO:47 (KLH2 domain g),
SEQ ID NO:48 (partial KLH2 domain h),
SEQ ID NO:63 (HtH1 domain a' + signal peptide),
SEQ ID NO:64 (HtH1 domain h'),
SEQ ID NO:65 (partial HtH2 domain a),

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SEQ ID NO:66 (HtH2 domain b'),
SEQ ID NO:67 (HtH2 domain d'),
SEQ ID NO:68 (HtH2 domain e'),
SEQ ID NO:69 (partial KLH1 domain b'),
SEQ ID NO:70 (KLH1 domain e'),
SEQ ID NO:71 (KLH1 domain f),
SEQ ID NO:72 (KLH1 domain g),
SEQ ID NO:73 (KLH1 domain h),
SEQ ID NO:74 (KLH2 domain b'),
SEQ ID NO:75 (KLH2 domain c'),
SEQ ID NO:76 (KLH2 domain d'),
SEQ ID NO:77 (KLH2 domain e),
SEQ ID NO:78 (KLH2 domain f),
SEQ ID NO:79 (KLH2 domain g'),

or a fragment of one of these sequences which has the immunological properties of at least one domain of a haemocyanin.

22. Recombinant haemocyanin polypeptide, obtainable by a process for the preparation of a haemocyanin polypeptide, wherein a nucleic acid molecule and/or a construct comprising said nucleic acid molecule is expressed in a suitable host cell and the protein is isolated, if appropriate, wherein said nucleic acid molecule comprising a nucleic acid molecule comprises a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),

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SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),
SEQ ID NO:80 (HtH1 domain a" + signal peptide),
SEQ ID NO:81 (HtH1 domain b"),
SEQ ID NO:82 (HtH1 domain c"),
SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),

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SEQ ID NO:98 (KLH1 domain d"),
 SEQ ID NO:99 (KLH1 domain e"),
 SEQ ID NO:100 (KLH1 domain f"),
 SEQ ID NO:101 (KLH1 domain g"),
 SEQ ID NO:102 (KLH2 domain b"),
 SEQ ID NO:103 (KLH2 domain c"),
 SEQ ID NO:104 (KLH2 domain d"),
 SEQ ID NO:105 (KLH2 domain e"),
 SEQ ID NO:106 (KLH2 domain f"),
 SEQ ID NO:107 (KLH2 domain g"),
 SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerated to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences

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described under (a) ;

(f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and

(g) combinations of several of the DNA sequences described under (a) to (f) or modifications thereof.

23. Recombinant haemocyanin polypeptide according to claim 22, **characterized in that** it comprises the sequences SEQ ID NO: 25 to 32 and is haemocyanin 1 from *Haliotis tuberculata*, it being possible for the sequence with SEQ ID NO:25 to be replaced by SEQ ID NO:63 and/or SEQ ID NO:32 to be replaced by SEQ ID NO:64.

24. Recombinant haemocyanin polypeptide according to claim 22, **characterized in that** it comprises either the sequences SEQ ID NO: 33 to 39 or the sequences SEQ ID NO:65, 66, 34-39 and is haemocyanin 2 from *Haliotis tuberculata*, it being possible in each case for SEQ ID NO:35 to be replaced by SEQ ID NO:67 and/or SEQ ID NO:36 to be replaced by SEQ ID NO:68.

25. Recombinant haemocyanin polypeptide according to claim 23, **characterized in that** it has an apparent

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molecular weight of 370 kDa in SDS-PAGE under
reducing conditions.

26. Recombinant haemocyanin polypeptide according to
claim 24, **characterized in that** it has an apparent
molecular weight of 370 kDa in SDS-PAGE under
reducing conditions.

27. Recombinant haemocyanin polypeptide according to
claim 21, **characterized in that** the haemocyanin
polypeptide comprises either the sequences SEQ ID NO:
40 to 43 or the sequences SEQ ID NO:40 to 43 and SEQ
ID NO:71 to 73 and is KLH1 from *Megathura crenulata*,
it being possible in each case the for sequence with
SEQ ID NO:40 to be replaced by SEQ ID NO:66 and/or
SEQ ID NO:43 to be replaced by SEQ ID NO:70.

28. Recombinant haemocyanin polypeptide according to
claim 21, **characterized in that** the haemocyanin
polypeptide comprises either the sequences SEQ ID NO:
44 to 48 or the sequences SEQ ID NO:44 to 46, 77, 78,
47, 48 and is KLH2 from *Megathura crenulata*, in being
possible in each case for the sequence with SEQ ID
NO:44 to be replaced by SEQ ID NO:74, SEQ ID NO:45 to
be replaced by SEQ ID NO:75, SEQ ID NO:46 to be
replaced by SEQ ID NO:76 and/or SEQ ID NO:47 to be
replaced by SEQ ID NO:79.

29. Recombinant haemocyanin polypeptide according to
claim 20, **characterized in that** it is bonded
covalently to viruses, virus constituents, bacteria,

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bacteria constituents, DNA, DNA constituents,
inorganic or organic molecules, such as e.g.
carbohydrates, peptides and/or glycoproteins.

30. Recombinant haemocyanin polypeptide according to
claim 20, **characterized in that** the haemocyanin
polypeptide is non-glycosylated.

31. Recombinant haemocyanin polypeptide according to
claim 20, **characterized in that** the haemocyanin
polypeptide is glycosylated.

32. Pharmaceutical composition, comprising a nucleic
acid molecule and/or a construct comprising said
nucleic acid molecule and physiologically tolerated
additives, wherein said nucleic acid molecule
comprises a nucleic acid sequence which codes for a
haemocyanin, a haemocyanin domain or a functional
fragment thereof with the immunological properties of
at least one domain of a haemocyanin, the nucleic
acid sequence being selected from:

(a) nucleic acid sequences which are selected from
the group consisting of the DNA sequences shown
below or the corresponding RNA sequences or which
contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),

SEQ ID NO:2 (HtH1 domain b),

SEQ ID NO:3 (HtH1 domain c),

SEQ ID NO:4 (HtH1 domain d),

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SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),

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SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerate to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin;
and

```
SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
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SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),
SEQ ID NO:52 (HtH2 domain d'),
SEQ ID NO:53 (HtH2 domain e'),
SEQ ID NO:54 (KLH1 domain e'),
SEQ ID NO:55 (KLH1 domain f),
SEQ ID NO:56 (KLH1 domain g),
SEQ ID NO:57 (KLH2 domain b'),
SEQ ID NO:58 (KLH2 domain c'),
SEQ ID NO:59 (KLH2 domain d'),
SEQ ID NO:60 (KLH2 domain e),
SEQ ID NO:61 (KLH2 domain f),
SEQ ID NO:62 (KLH2 domain g'),

(b) nucleic acid sequences which hybridize with the

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counter-strand of a nucleic acid sequence
according to (a) and code for a polypeptide which
has the immunological properties of at least one
domain of a haemocyanin;

(c) nucleic acid sequences which on the basis of the
genetic code are degenerated to the DNA sequences
defined under (a) and (b) and code for a
polypeptide which has the immunological properties
of at least one domain of a haemocyanin;

(d) nucleic acid sequences which hybridize with one
of the nucleic acid sequences described under (a)
to (c) and the counter-strand of which codes for a
polypeptide which has the immunological properties
of at least one domain of a haemocyanin;

(e) nucleic acid sequences which are at least 60%
homologous to one of the nucleic acid sequences
described under (a);

(f) variants of the sequences described under (a) to
(d), the variants containing additions, deletions,
insertions or inversions with respect to the
sequences described under (a) to (d) and coding
for a polypeptide which has the immunological
properties of at least one domain of haemocyanin;
and

(g) combinations of several of the DNA sequences
described under (a) to (f).

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35. Pharmaceutical composition according to claim 34, **characterized in that** it is used as an antiparasitic composition, antiviral composition or as an antitumour composition.

36. Pharmaceutical composition according to claim 34, **characterized in that** it is used for treatment of one of the following diseases: schistosomiasis, high blood pressure, surface bladder carcinomas, epithelial carcinomas, ovarian carcinoma, mammary carcinoma, bronchial carcinoma and colorectal carcinoma.

37. Pharmaceutical composition according to claim 34, **characterized in that** it is used as a vaccine.

38. Pharmaceutical composition according to claim 34, **characterized in that** it is used for prevention of cocaine abuse.

39. Use of a haemocyanin polypeptide as a carrier substance for medicaments, wherein said haemocyanin polypeptide comprises an amino acid sequence which is coded by one or more of the nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(a) nucleic acid sequences which are selected from

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),
SEQ ID NO:14 (HtH2 domain g),
SEQ ID NO:15 (HtH2 domain h),
SEQ ID NO:16 (partial KLH1 domain b),
SEQ ID NO:17 (KLH1 domain c),
SEQ ID NO:18 (KLH1 domain d),
SEQ ID NO:19 (partial KLH1 domain e),
SEQ ID NO:20 (KLH2 domain b),
SEQ ID NO:21 (KLH2 domain c),
SEQ ID NO:22 (partial KLH2 domain d),
SEQ ID NO:23 (KLH2 domain g),
SEQ ID NO:24 (partial KLH2 domain h),
SEQ ID NO:49 (HtH1 domain a' + signal peptide),
SEQ ID NO:50 (partial HtH2 domain a),
SEQ ID NO:51 (HtH2 domain b'),

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(f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and

(g) combinations of several of the DNA sequences described under (a) to (f).

40. Liposome, comprising a nucleic acid molecule , a construct comprising said nucleic acid molecule and/or a haemocyanin polypeptide encoded by said nucleic acid molecule, wherein said nucleic acid molecule comprises a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(a) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),

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SEQ ID NO:6 (HtH1 domain f),
 SEQ ID NO:7 (HtH1 domain g),
 SEQ ID NO: 8 (HtH1 domain h),
 SEQ ID NO:9 (partial HtH2 domain b),
 SEQ ID NO:10 (HtH2 domain c),
 SEQ ID NO:11 (HtH2 domain d),
 SEQ ID NO:12 (HtH2 domain e),
 SEQ ID NO:13 (HtH2 domain f),
 SEQ ID NO:14 (HtH2 domain g),
 SEQ ID NO:15 (HtH2 domain h),
 SEQ ID NO:16 (partial KLH1 domain b),
 SEQ ID NO:17 (KLH1 domain c),
 SEQ ID NO:18 (KLH1 domain d),
 SEQ ID NO:19 (partial KLH1 domain e),
 SEQ ID NO:20 (KLH2 domain b),
 SEQ ID NO:21 (KLH2 domain c),
 SEQ ID NO:22 (partial KLH2 domain d),
 SEQ ID NO:23 (KLH2 domain g),
 SEQ ID NO:24 (partial KLH2 domain h),
 SEQ ID NO:49 (HtH1 domain a' + signal peptide),
 SEQ ID NO:50 (partial HtH2 domain a),
 SEQ ID NO:51 (HtH2 domain b'),
 SEQ ID NO:52 (HtH2 domain d'),
 SEQ ID NO:53 (HtH2 domain e'),
 SEQ ID NO:54 (KLH1 domain e'),
 SEQ ID NO:55 (KLH1 domain f),
 SEQ ID NO:56 (KLH1 domain g),
 SEQ ID NO:57 (KLH2 domain b'),
 SEQ ID NO:58 (KLH2 domain c'),
 SEQ ID NO:59 (KLH2 domain d'),
 SEQ ID NO:60 (KLH2 domain e),

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- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (c) nucleic acid sequences which on the basis of the genetic code are degenerate to the DNA sequences defined under (a) and (b) and code for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (d) nucleic acid sequences which hybridize with one of the nucleic acid sequences described under (a) to (c) and the counter-strand of which codes for a polypeptide which has the immunological properties of at least one domain of a haemocyanin;
- (e) nucleic acid sequences which are at least 60% homologous to one of the nucleic acid sequences described under (a);
- (f) variants of the sequences described under (a) to (d), the variants containing additions, deletions, insertions or inversions with respect to the sequences described under (a) to (d) and coding for a polypeptide which has the immunological properties of at least one domain of haemocyanin; and
- (g) combinations of several of the DNA sequences

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described under (a) to (f).

41. Liposome according to claim 40, **characterized in that** the liposome furthermore comprises cell recognition molecules.

42. Antibodies, obtainable by immunization of a test animal with a recombinant haemocyanin polypeptide comprising an amino acid sequence which is coded by one or more of the nucleic acid molecule comprising a nucleic acid sequence which codes for a haemocyanin, a haemocyanin domain or a functional fragment thereof with the immunological properties of at least one domain of a haemocyanin, the nucleic acid sequence being selected from:

(a) nucleic acid sequences which are selected from the group consisting of the DNA sequences shown below or the corresponding RNA sequences or which contain these:

SEQ ID NO:1 (HtH1 domain a + signal peptide),
 SEQ ID NO:2 (HtH1 domain b),
 SEQ ID NO:3 (HtH1 domain c),
 SEQ ID NO:4 (HtH1 domain d),
 SEQ ID NO:5 (HtH1 domain e),
 SEQ ID NO:6 (HtH1 domain f),
 SEQ ID NO:7 (HtH1 domain g),
 SEQ ID NO: 8 (HtH1 domain h),
 SEQ ID NO:9 (partial HtH2 domain b),
 SEQ ID NO:10 (HtH2 domain c),

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SEQ ID NO:11 (HtH2 domain d),
 SEQ ID NO:12 (HtH2 domain e),
 SEQ ID NO:13 (HtH2 domain f),
 SEQ ID NO:14 (HtH2 domain g),
 SEQ ID NO:15 (HtH2 domain h),
 SEQ ID NO:16 (partial KLH1 domain b),
 SEQ ID NO:17 (KLH1 domain c),
 SEQ ID NO:18 (KLH1 domain d),
 SEQ ID NO:19 (partial KLH1 domain e),
 SEQ ID NO:20 (KLH2 domain b),
 SEQ ID NO:21 (KLH2 domain c),
 SEQ ID NO:22 (partial KLH2 domain d),
 SEQ ID NO:23 (KLH2 domain g),
 SEQ ID NO:24 (partial KLH2 domain h),
 SEQ ID NO:49 (HtH1 domain a' + signal peptide),
 SEQ ID NO:50 (partial HtH2 domain a),
 SEQ ID NO:51 (HtH2 domain b'),
 SEQ ID NO:52 (HtH2 domain d'),
 SEQ ID NO:53 (HtH2 domain e'),
 SEQ ID NO:54 (KLH1 domain e'),
 SEQ ID NO:55 (KLH1 domain f),
 SEQ ID NO:56 (KLH1 domain g),
 SEQ ID NO:57 (KLH2 domain b'),
 SEQ ID NO:58 (KLH2 domain c'),
 SEQ ID NO:59 (KLH2 domain d'),
 SEQ ID NO:60 (KLH2 domain e),
 SEQ ID NO:61 (KLH2 domain f),
 SEQ ID NO:62 (KLH2 domain g'),
 SEQ ID NO:80 (HtH1 domain a" + signal peptide),
 SEQ ID NO:81 (HtH1 domain b"),
 SEQ ID NO:82 (HtH1 domain c"),

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SEQ ID NO:83 (HtH1 domain d"),
SEQ ID NO:84 (HtH1 domain e"),
SEQ ID NO:85 (HtH1 domain f"),
SEQ ID NO:86 (HtH1 domain g"),
SEQ ID NO:87 (HtH1 domain h"),
SEQ ID NO:88 (partial HtH2 domain a"),
SEQ ID NO:89 (HtH2 domain b"),
SEQ ID NO:90 (HtH2 domain c"),
SEQ ID NO:91 (HtH2 domain d"),
SEQ ID NO:92 (HtH2 domain e"),
SEQ ID NO:93 (HtH2 domain f"),
SEQ ID NO:94 (HtH2 domain g"),
SEQ ID NO:95 (HtH2 domain h"),
SEQ ID NO:96 (partial KLH1 domain b"),
SEQ ID NO:97 (KLH1 domain c"),
SEQ ID NO:98 (KLH1 domain d"),
SEQ ID NO:99 (KLH1 domain e"),
SEQ ID NO:100 (KLH1 domain f"),
SEQ ID NO:101 (KLH1 domain g"),
SEQ ID NO:102 (KLH2 domain b"),
SEQ ID NO:103 (KLH2 domain c"),
SEQ ID NO:104 (KLH2 domain d"),
SEQ ID NO:105 (KLH2 domain e"),
SEQ ID NO:106 (KLH2 domain f"),
SEQ ID NO:107 (KLH2 domain g"),
SEQ ID NO:108 (partial KLH2 domain h");

- (b) nucleic acid sequences which hybridize with the counter-strand of a nucleic acid sequence according to (a) and code for a polypeptide which has the immunological properties of at least one

SEQ ID NO:1 (HtH1 domain a + signal peptide),
SEQ ID NO:2 (HtH1 domain b),
SEQ ID NO:3 (HtH1 domain c),
SEQ ID NO:4 (HtH1 domain d),
SEQ ID NO:5 (HtH1 domain e),
SEQ ID NO:6 (HtH1 domain f),
SEQ ID NO:7 (HtH1 domain g),
SEQ ID NO: 8 (HtH1 domain h),
SEQ ID NO:9 (partial HtH2 domain b),
SEQ ID NO:10 (HtH2 domain c),
SEQ ID NO:11 (HtH2 domain d),
SEQ ID NO:12 (HtH2 domain e),
SEQ ID NO:13 (HtH2 domain f),

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SEQ ID NO:14 (HtH2 domain g),
 SEQ ID NO:15 (HtH2 domain h),
 SEQ ID NO:16 (partial KLH1 domain b),
 SEQ ID NO:17 (KLH1 domain c),
 SEQ ID NO:18 (KLH1 domain d),
 SEQ ID NO:19 (partial KLH1 domain e),
 SEQ ID NO:20 (KLH2 domain b),
 SEQ ID NO:21 (KLH2 domain c),
 SEQ ID NO:22 (partial KLH2 domain d),
 SEQ ID NO:23 (KLH2 domain g),
 SEQ ID NO:24 (partial KLH2 domain h),
 SEQ ID NO:49 (HtH1 domain a' + signal peptide),
 SEQ ID NO:50 (partial HtH2 domain a),
 SEQ ID NO:51 (HtH2 domain b'),
 SEQ ID NO:52 (HtH2 domain d'),
 SEQ ID NO:53 (HtH2 domain e'),
 SEQ ID NO:54 (KLH1 domain e'),
 SEQ ID NO:55 (KLH1 domain f),
 SEQ ID NO:56 (KLH1 domain g),
 SEQ ID NO:57 (KLH2 domain b'),
 SEQ ID NO:58 (KLH2 domain c'),
 SEQ ID NO:59 (KLH2 domain d'),
 SEQ ID NO:60 (KLH2 domain e),
 SEQ ID NO:61 (KLH2 domain f),
 SEQ ID NO:62 (KLH2 domain g'),
 SEQ ID NO:80 (HtH1 domain a" + signal peptide),
 SEQ ID NO:81 (HtH1 domain b"),
 SEQ ID NO:82 (HtH1 domain c"),
 SEQ ID NO:83 (HtH1 domain d"),
 SEQ ID NO:84 (HtH1 domain e"),
 SEQ ID NO:85 (HtH1 domain f"),

(c) nucleic acid sequences which on the basis of the

characterized in that the tumour to be detected is a bladder carcinoma, epithelial carcinoma, ovarian

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carcinoma, mammary carcinoma, bronchial carcinoma or
colorectal carcinoma.

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Markl, et al.

§ 371 Patent Application of PCT/EP00/02410
filed September 17, 2001

test animal with haemocyanin, a haemocyanin domain, a
fragment thereof or a fusion protein, and the use
thereof in screening methods for the identification
of tumours.

Fig. 1a-f

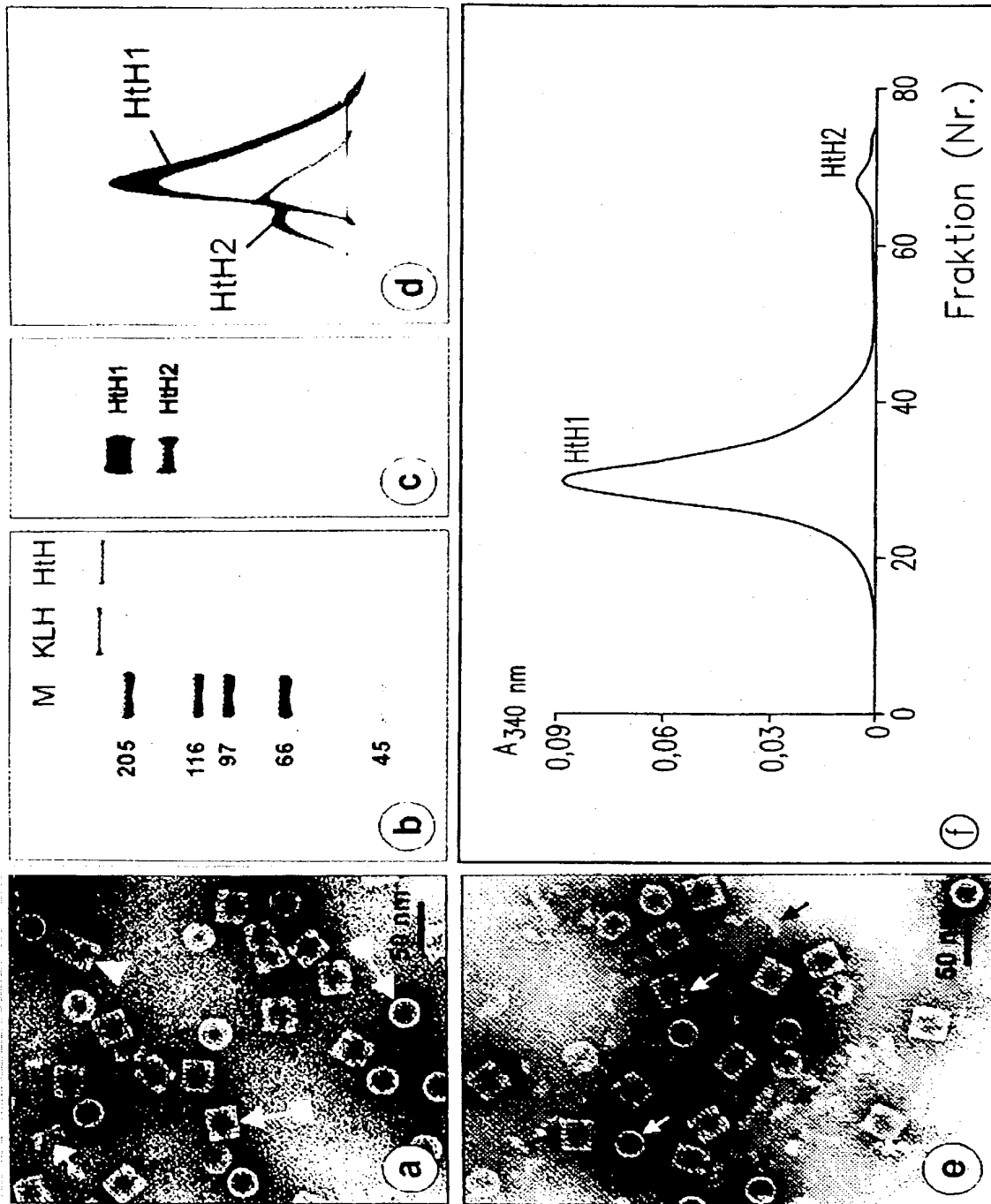


Fig. 1g-m

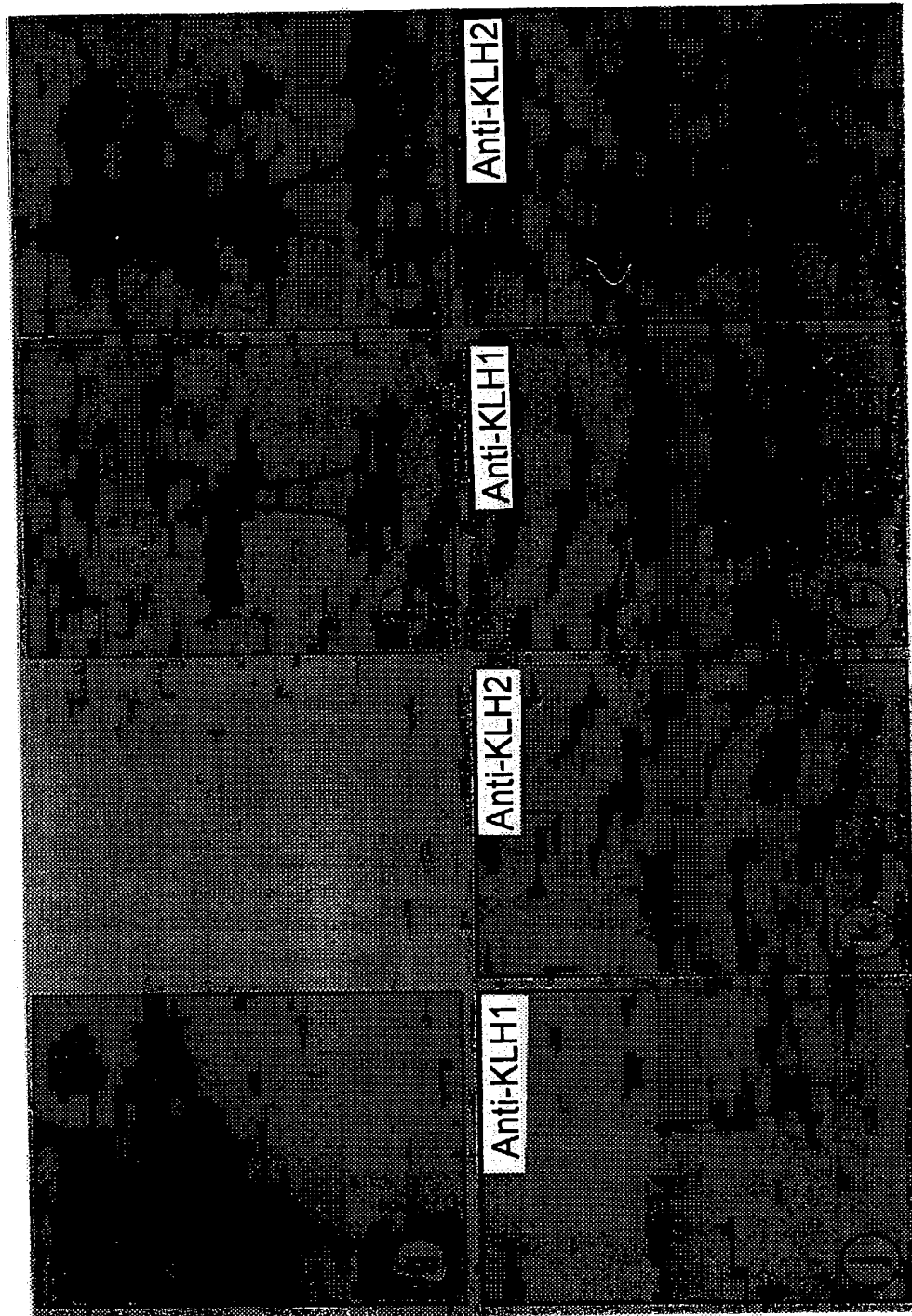


Fig. 2a-h

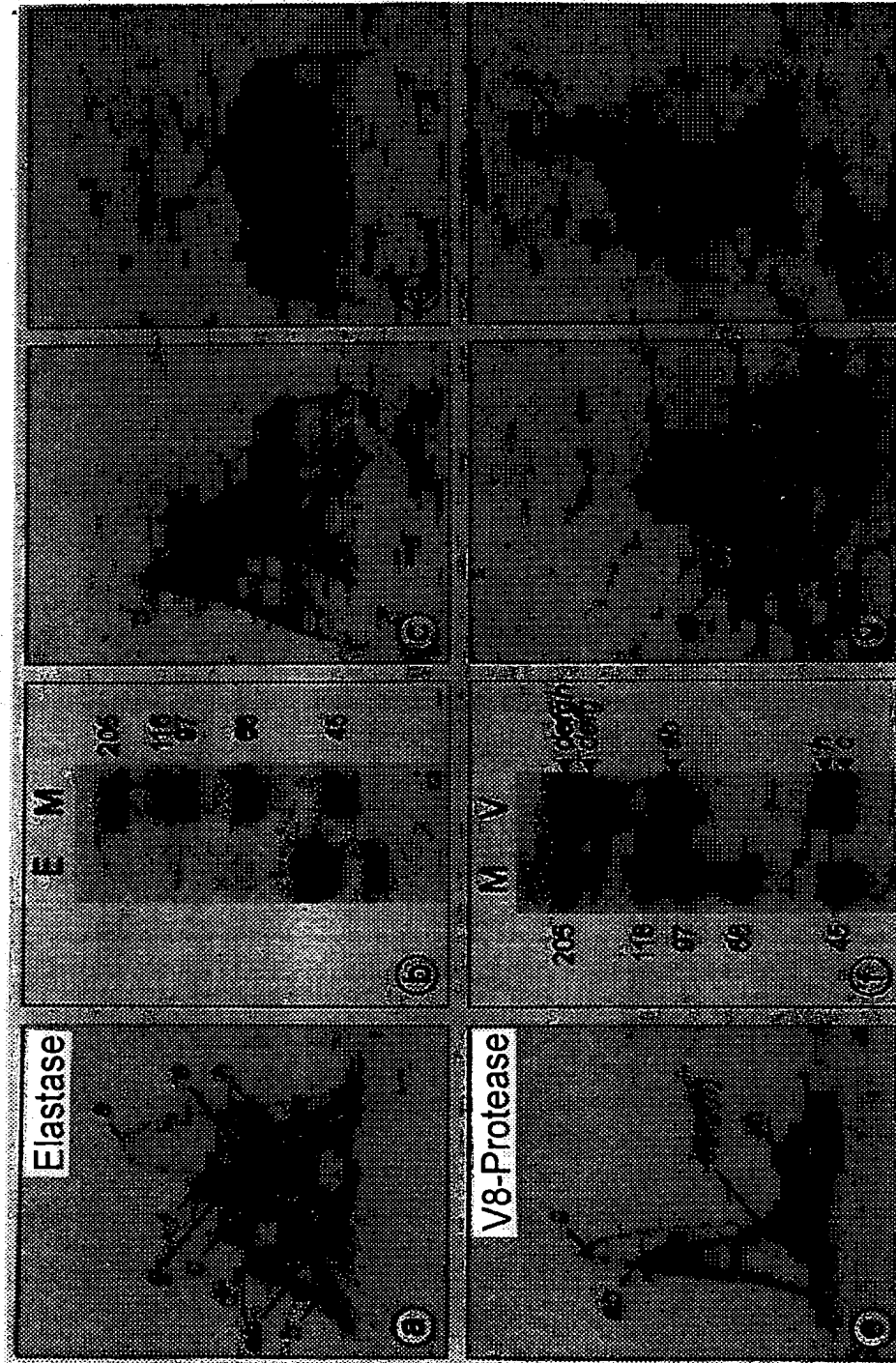
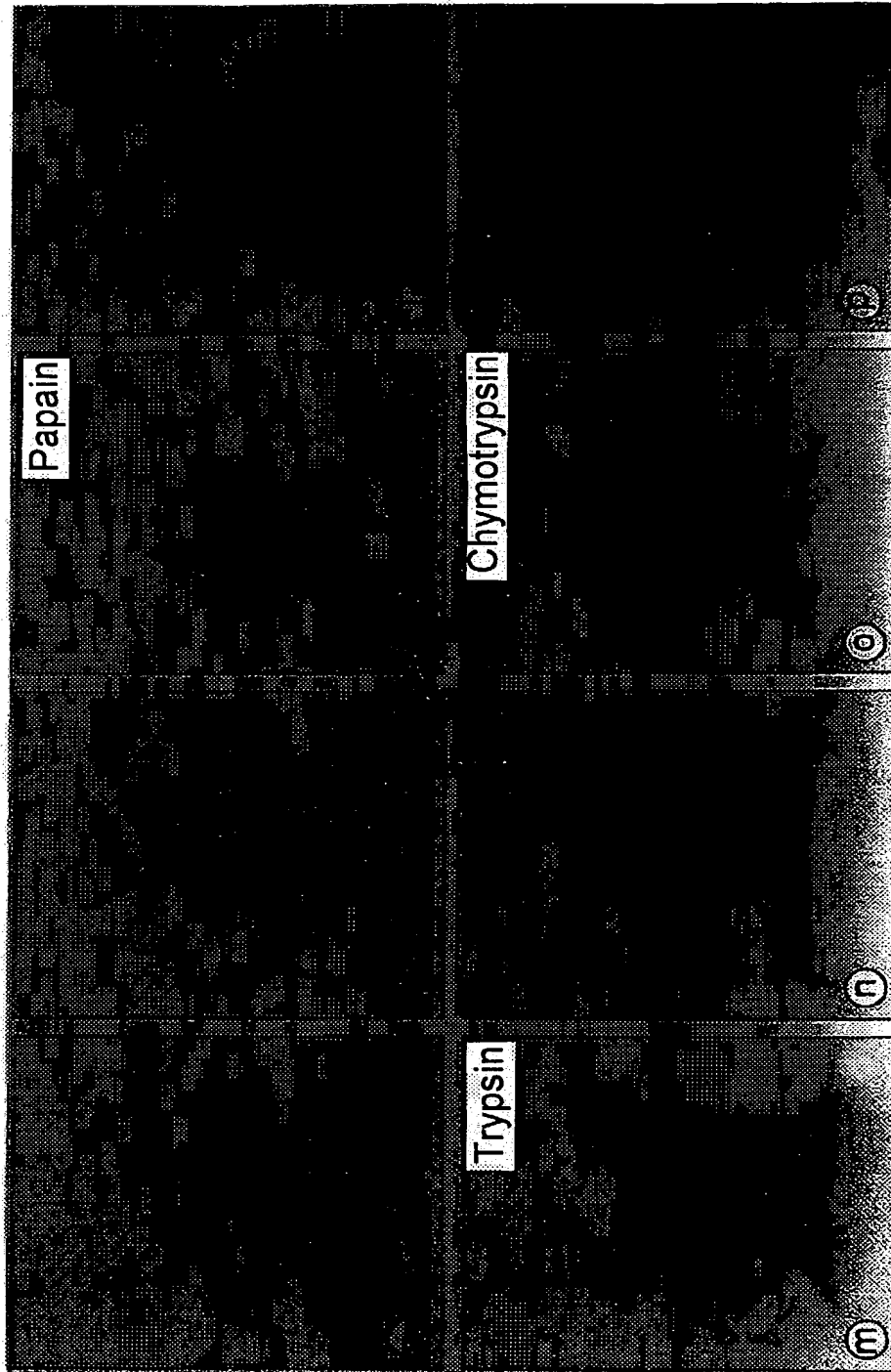
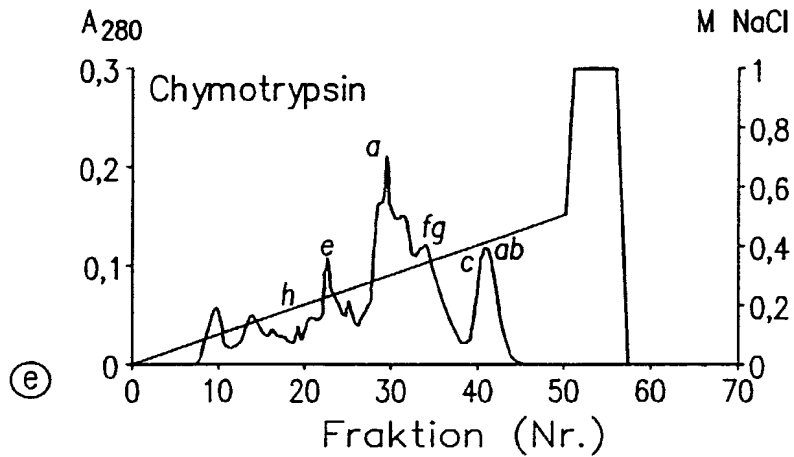
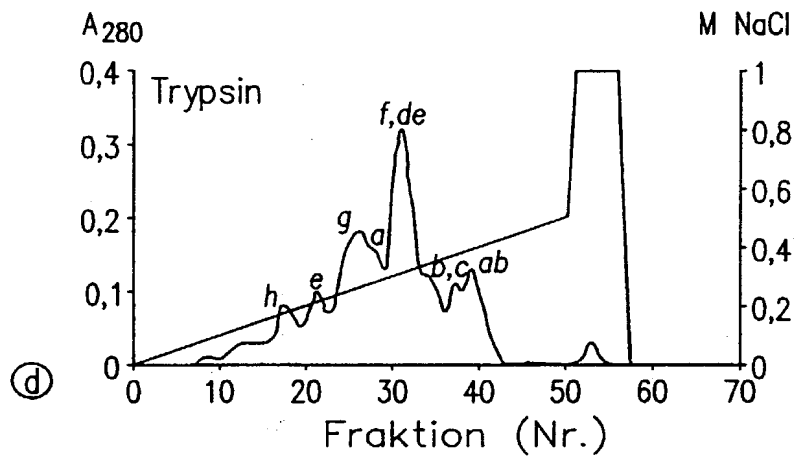


Fig. 2i-p



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Fig. 3d-e



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Figur 4

cDNA-Sequenz in Verbindung mit Intronstruktur des HtH1

Domäne a

GGCTTGTTTCAGTTTCTACTCGTCGCCCTTGTGGCGGGGGCTGGAGCAGACAACGTCGTCAG
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Domäne b

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Intron b/c

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TAGTCLTCTAATATAATCATTTTCGATAAATACTTTGGGCAACAAATCAATGTAACATCT
ATTTTCTTTTCAG

Domäne c

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Intron c/d

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Domäne d

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Intron d/e

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Domäne e

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Intron e/f

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Domäne \mathbb{R}^n

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Domäne $\mathbb{R} \setminus (2)$

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Intron f/g

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Domäne g(1)

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ACAACCCCTTCCAAACAT

Intron g(2)

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Domäne g(2)

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Intron g/h

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Domäne h

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3' UTR

TTCACAG

Intron UTR

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GCAGTTACACCATCGACATTTCCAACCTCCTCAGAACTAATATATAGCCTTAATACAACC
AGCCAAGACTCAACGGGCAGCCGGGGTGGGGGGATTGTTGGTGGTGGCTGTTTCAGACCAGGG
TGCAAAATATCAGTGCGCAATCAACATGTTGCGTGTGACACACTGACACAGCAGTCATTG
AACCTGCAGACCCATAACAGGAAATGGGGGCAGATACGATCAAGACAGTGTAAATAGGG
ATAAGTAGGCATATGCAACCACCTGATGGAAATGAAAAGGGGTAAAGTTTAAACCCCGGCTA
CCAAAGGTCCAATGGTTCCCTTAACCCAGCTTACGCTATCCCTCTAATTTTCAGTATTGAGCT
GATTTCTGTGAGTTTCATGTAACTGTATACTTTCTGTATTATTACAG

3' UTR

GTTGCTATGCCGACTGCGCTATATTGGTGAACGAGACGATGAGGACATCTCTGAAAGAGTT
CGCCAAGTGATGTGTAGGTACCGGAAGTATTGTTGAGCTAACAATATGATGATTTCLAAAT
GACTTGGCGCTCTAGGACAAAGACATAATTCATCAGCACCCCTGTGCACCAACTCTTTGTTT
GCTGCAACGCTCTGACAAGCGACACGTCAATCAACAAGCTGTTCAAACCTCAAGTGGATGTA
ACTAGAATCGTTGGGGCCATCGTTCACAAAGTATTGACAGATGTCACACATGATGGCGAGAA
ACACTTTAGAATTTTAAATGACCTAGAGTGACTTGTAATATGTAAATATATTCTTCAAAG
ACTCAGCTGAATATTGTTGGATAACACATCAATTCCTCAACAAAATGCTTTATCTTCAC
ATGGATGTATGTAATGTGGCCGGCAATAAAGTATATATATGTATAAAAAAAAAAAAAAAAA
A

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Figur 5

Abgeleitete Primärstruktur des HtH1

Signalpeptid

LVQFLLVAGAGA

Domäne a

DNVVRKDVSHLTDDDEVQALHGALHDVTASTGPLSFEDITSYHAAPASCDYKGRKIAACCVHG
MPSPFPWHRAYVVOAERALLSKRKTVGMPYWDWTQTLTHLPSLVTEPIYIDSKGGKAQNTY
WYRGEIAFINKKTARAVDDRLFEKVEPGHYTHLMTVLDALQDEFCKFETIQFELAHNAIH
YLVGGKFEYSMSNLEYTSYDPIFFLHRSNVDRLFAIWQRLQELRGKNPNAMDCAHSLAHQQ
LQPFNRDSNPVQLTKDHSTPADLFDYKQLGYSYDSLNLNGMTPEQLKTELDERHSKERAF
SFRLSGFGGSANVVVYACVPDDDDPRSDDYCEKAGDFFILGGQSEMPWRFYRPTFYDVTEAV
HHLGVPLSGHYVVKTELFVNGTALSPDLLPQPTVAYRPGK

Domäne b

GHLDPVHHRHDDDLIVRKNI DHLTREEEYELRMALERFOADTSVDGYQATVEYHGLPARC
PRPDAKVRFACCMHGMASFPHWHRLFVTQVEDALVRRGSPIGVPYWDWTKPMTHLPDLASN
ETYVDPYGHTRHNPFNANISFEEGGHHTSRMIDSKLFAPVAFGEHSHLFDGILYAFEQED
FCDFEIQFELVHNSIHAWIGGSESYMATLHYTAFDPIFYLHHSNVDRLWAIWQALQIRRH
KPYQAHCAQSVEQLPMKPFAPPSPLNNEKTHSHSVPTDIYDYEEVLHYSYDDLTFGGMNL
EEIEBAIHLRQQHERVFAGFLLAGIGTSALVDIFINKPGNQPLKAGDIAILGGAKEMPWAF
DRLYKVEITDSLKTLSLDVGDYEVTFKIHDMHGNAIDTDLI PHAAVVSEPAH

Domäne c

PTFEDEKHS LRIRKNVDSLTP EETNELRKALELLENDHTAGGFNQLGAFHGE PKWCPNPEA
EHKVACCVHGMVFPWHRLALQENALRKHGYS GALPYWDWTRPLSOLPDLVSHEQYTD
PSDHHVKHNPWFNGHIDTVNQDTTRS VREDLYQQPEFGHFTDIAQQVLLALEQDDFCSEV
QYEISHNFIALVGGT DAYGMASLRYTAYDPIFFLHHSNTDRIWAIWQSLQYRGKPYNTA
NCAIESMRRP LQPFGLSSAINPDRTREHAI PFDVFNRYRDNLHYVYDTLEFNGLSISQLDR
ELEKIKSHERVFAGFLLSGIKKSALVKFEVCTPPDNCHKAGEFYLLGDENEMAWAYDRLEK
YDITQVLEANHLEFYDHLFIRYEVFDLKGVS LGTDLFHTANVVHDSGT

Domäne d

GTRDRDNYVEEVTGASHIRKNLNDLNTGEMESLRAAFLHIQDDGTYESIAQYHGKPGKCQL
NDHNIACCVHGMPTFPQWHRLYVQVENALLNRGSGVAVPYWEWTAPIDHLPHFIDDATYF
NSRQORYDPNPFFRGKVT FENAVTTRDPQAGLPNSDYMYENVLLALEQENYCDFEIQFELV
HNALHSM LGGKGQYSMSLLDYSAFDPVFFLHHANTDRLWAIWQELQRFREL PYEEANCAN
LMHQPLKPFSDPHENHDNVTLYSKPQDGFQYQNHFGYKYDNLEFHLSIPSLDATLKQRR
NHDRVFAGFLLHNIGTSADITIYICLPDGRRGNDCSHEAGTFYILGGGETEMPFIFDRLYKF
EITKPLQQLGVKLHGGVFELBLEIKAYNGSYLDPHTFDPTIIFEPGT

Domäne e

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DTHILDHDHEEEILVRKNIIDLSPRERSVLVKALQRMKNDRSADGYQAIASFHALPPLCPN
 PSAAHRYACCVHGMATFPQWHRLYTVQVQDALRRHGSLVGI PYWDWTKPVNELPELLSSAT
 FYHPIRNINISNPFLGADIEFEGPGVHTERHINTERLFHSGDHDGYHNWFFETVLFALQE
 DYCDFEIQFEIAHNGIHTWIGGS AVYGMGHLHYASYDPIFYIHHSQTDRIWAIWQELQKYR
 GLSGSEANCAIEHMRTPLKPFSGPPYNLNSHTOEYSKPEDTFDYKKFGYRYDSLELEGRS
 ISRIDELIQORQEKDRTFAGFLLKGFGTSASVSLQVCRVDHTCKDAGYFTILGGS AEMPWA
 FDRLYKYDITKTLHDMNLRHEDTFSIDVTITSYNGTVLSGDLIQTPSII FVPGR

Domäne f

HKLNSRKHTPNRVRHELSSLSRDIASLKAALTS LQHDNGTDGYQAI AAFHGVPAQCHEPS
 GREIACCIHGMATFPWHRLYTLQLEQALRRHGSSVAVPYWDWTKPITELPHILT DGEYYD
 VWQNAVLANPFGARGYVKIKDAFTVRNVQESL FKMSSFGKHSLLFDQALLALEQTDYCDFEV
 QFEVMHNTIHYLVGGRTYAFSSLEYSSYDPIFFI HHSFVDKIWAVWQELQSRRHLQFRTA
 DCAVGLMQAMRPFENKDFNHSFTKKHAVPNTVFDYEDLGYN YDNLEISGLNLNEIEALIA
 KRKSHARVFAGFLLFGLGTSADIHLEICKTSENCHDAGVIFILGGS AEMHWAYNRLKYDI
 TEALQEFDINPEDVPHADEPFFELRLSVVAVNGTVIPSSHLHQPTIITYEPGE

Domäne g

DHDDHQS GSGSIAGSGVRKDVNTLTKAETDN LREALWGVMA DHGPNGFQAI AAFHGKPALCP
 MPDGHNYSCC THGMATFPWHRLYTKQMEDAMRAH GSHVGLPYWDWTAAFTHLPTLVTDTD
 NNPFOHGHIDYLVNSTTRS PRDMLFNDPEHGSES FFYRQVLLALEQTD FCKFEVQFEITHN
 AIHSWTGGHSPYGMSTLDFTAYDPLFWLHHSNTDRIWAVWQALQ EYRGLPYNHANCEIQAM
 KTPLRPFSDDINHNPNVTKANAKPLDVFEYNRLS FQYDNLI FHGYSIPELDRVLEERKEEDR
 IFAAFLLSG IKR SADVVFDICQPEHECVFAGTFAILGGELEMPWSFDRLFRYDITKVMKQL
 HLRHDSDFTRVKIVGTDDHELPSDSVKAPTIEFEPG

Domäne h

VERGGNHEDEHDDRLADVLIRKEVD FLSLQEANA IKDALYKLQND DSKGGFEAIAGYHGY
 PNMCPERGT DKYPCCVHGMPVFPWHERLHTIQMERALKNHGS PMGI PYWDWTKKMSSLP SF
 FGDSSNNNP FYKYIRGVQHETTRDVNQRLFNQTKFGEFDYLYLT LQVLEENSYCDFEVQ
 YEILHNAVH SWLGGTGQYS MSTLEYS AFDPVFMIHSSLDRIWILWQKLQKIRMKPYALD
 CAGDRLMKDPLHPFN YETVNEDEFTRINS FPSILFDHYRFN YEYDNMRIRGQDIHELEEV
 QELRNKDRI FAGFVLSGLRISATVKVFIH SKNDTSHEEYAGEFAVLGGEKEMPWAYERMLK
 LDISDAVHKLHVKDEDIRFRVVVTAYNGDVVTTRLSQPFIVHRPAHVAHDI LVI PVGAGHD
 LPPKVVKSGTKVEFTPIDSSVN KAMVELG SYTAMAKCIVPPFSYHGFELDKVYSVDHGDY
 YIAAGTHALCEQNLRLHIHVEHE

Figur 6

cDNA-Sequenz in Verbindung mit Intronstruktur des HtH2

Domäne b

CACAGACTGTTCTGTCACCCAGGTGGAAGATGCTCTGATCAGGCGAGGATCGCCTATAGGGG
TCCCCCTACTGGGACTGGACTCAGCCTATGGCGCATCTCCAGGACTTGCAGACAACGCCAC
CTATAGAGATCCCATCAGCGGGGACAGCAGACACAACCCCTTCCACGATGTTGAAGTTGCC
TTTGAAATGGACGTACAGAACGTCACCCAGATAGTAGATTGTTTGAACAACCTTTATTG
GCALACATAACGCTCTCTTCGACAGTATAGTCTATGCTTTTGAGCAGGAGGACTTCTGGA
TTTTGAAGTTCAATTTGAGATGACCCATAATATATTCACGCCTGGATTGGTGGCGGGGAG
AAGTATTCATGTCTCTCTACACTACACAGCCTTCGACCCCTATCTTCTACCTTCGTCAC
CCAACACTGACCGGCTCTGGGCAATTTGGCAAGCGTTGCAGATACGAAGAAACAGGCCTTA
CAAGGCTCATTTGTGCTTGGTCTGAGGAACGCCAGCCTCTCAAACCTTTGCGCTTCAGTTCC
CCACTGAACACCAACGAAAAACCTACGAAAACTCGGTGCCACCAACGTTTACGACTACG
AAGGAGTCCTTGGCTATACTTATGATGACCTCAACTTCGGGGGCATGGACCTGGGTACGCT
TGAGGAATACATCCAGAGGCAGAGACAGAGAGACAGGACCTTTGCTGGTTTCTTTCTGTCA
CATATTTGGTACATCAGCGAATGTTGAATCATTTATAGACCATGGGACTCTTCATACCTCCG
TGGGCACGTTTGGCTGTTCTTGGCGGAGAGAAAGGAGATGAAATGGGGATTTGACCGTTTGT
CAATATGAGATTACAGATGAACGAGGCAACTTAATCTCCGTGCTGATGATGTTTTTCAGC
ATCTCTGTTAAAGTAACTGATGTTGATGGCAGTGAGCTGTCTCTGAACTCATCCCATCTG
CTGCTATCATCTTCGAACGAAGCCATA

Intron b/c

GTAAGTAGCTACCTGTTTATTCAATTTTTTCGCTTTGCCAATCAATTCATTCAGCTTGAAA
TTCAATAAATTGTGTTTTGCATGGCTGAAAACCAATTTGAACTCTTTTCTTTCTCAGGTGG
AACTCAAATAAATAATCACTAATTGTTATGCACGCGGGTAGGGCATACTATATCCAC
ATCGGTATCTCAAAATGCAAAACAATTTGTCTTATTTCCGTTGGGGACAAGCAAAACCCCTT
TCCTGTAATCTTGCCTTTGGCATCCACTGGAATTAATGTTGACTGGTAATTTGATACTGGCT
CTCTTCTTGCATAGAGTTAATATCTATAGTTTGTAAATCTTTATGATTTTGCTATTTATAT
TTGACAGCATGCTATAGACACCCTAGACTATTGTATAGCCACTTGTATTGTTTTTCCATT
TATTATTTATAACAGAACATGGCTTGTAAATTTTTATTTACCTTCCAG

Domäne c

TTGACCATCAGGACCCCGCATCATGACACAATCATTAGGAAAAATGTTGATAATCTTACACC
CGAGGAAATTAATTCTCTGAGGCGGGCAATGGCAGACCTTCAATCAGACALAACCGCCGGT
GGATTCCAGCAAATTGCTGCTTTTCACGGGGAAACCCAAATGGTGCCCAAGTCCCGATGCTG
AGAAGAAGTTCTCTGCTGTGTCCATGGAATGGCTGTCTTCCCTCACTGGCACAGACTCCT
GACCGTGCAAGGCGAGAATGCCCTGAGAAAGCATGGATGTCTCGGAGCTCTCCCTACTGG
GACTGGACTCGGCCCTGTCTCACCTACCTGATTTGGTTTTGGTAAGTAGCAGAACTACAC
CGATGCCATATTCCACCGTGGAAGCCCGAAACCCCTGGTACAGCGGCCATATTGATACAGT
TGGTGTGACACACAAGAAGCGTCCGTCAAGAAGTGTATGAAGCTCCTGGATTGTGCCAT
TATACTGGGGTGGCTAAGCAAGTGCTTCTGGCTTTGGAGCAGGATGACTTCTGTGATTTTG
AAGTCCAGTTTGAATAGCTCACAAATTCATTCACGCTCTTGTGGCGGGAAGCGAGCCATA
TGGTATGGCGTCACTCCGTTACACTACTTATGATCCAATTTTCTACCTCCATCATTTCTAAC
ACTGCAGAGACTCTGGGCTATATGGCAGGCTCTACAAAAGTACAGGGGCAAACCTTACAATT
CGGCCAATGCGCCATTGCTTCTATGAGAAAACCCCTACAACCCTTTGGTCTGACTGATGA
GATCAACCCGGATGATGAGACAAGACAGCATGTCTGTTCTTTCAGTGCTCTTGAACAAG
AACAACTTCAATTATGAATATGACACCCTTGACTTCAACGGACTATCAATCTCCAGCTGG
ACCGTGAAGTGTACGGAGAAAGTCTCATGACAGAGTATTTGCCGGATTTTGTCTGCATGG

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TATTCAGCAGTCTGCACTAGTTAAATTCTTTGTCTGCAAATCAGATGATGACTGTGACCAC
TATGCTGGTGAATTCTACATCCTTGGTGATGAAGCTGAAATGCCATGGGGCTATGATCGTC
TTTACAAATATGAGATCACTGAGCAGCTCAATGCCCTGGATCTACACATCGGAGATAGATT
CTTCATCAGATACGAAGCGTTTGATCTTCATGGTACAAGTCTTGGAAGCAACATCTTCCCC
AAACCTTCTGTCTATACATGACGAAGGGGCAG

Intron c/d

GTGAGAACATTGATAATAGTTCAAATGAAGTATATCCGATTCAAGCTGTGCGATACAAGATG
AGATACATAATCACAATGTTTGTATTAGATATCTCTCTTAATTTAATGCCGCTTTTATCAA
TATTCGAGCAATCCTTCAGCAACATACACCAGCAATGTTTCATCAACAGACTATATTATT
TAATCTTTTAAAAATCCTTTTCTGTTGTTATAAATACTTAAAGTATCGAATTCCTTGAATG
CGTCTTCTCTGCAAGCATATAGTTAAGTTGTTGTGTTTCTCTGTCTAG

Domäne d

GTCACCATCAGGCTGACGAGTACGACGAAGTTGTAAGTCTGCAAGCCACATCAGAAAGAA
TTTAAAGATCTGTCAAAGGGAGAAGTAGAGAGCCTAAGGTCTGCCTTCCTGCAACTTCAG
AACGACGGAGTCTATGAGAATATTGCCAAGTTCCACGGCAAGCCTGGGTTGTGTGATGATA
ACGGTCGCAAGGTTGCCTGTTGTGTCCATGGAATGCCACCTTCCCCCAGTGGCACAGGCT
CTATGTCCTCCAGGTGGAGAATGCTTTGCTGGAGAGAGGATCTGCCGTCTCTGTGCCATAC
TGGGACTGGACTGAAACATTTACAGAGCTGCCATCTTTGATTGCTGAGGCTACCTATTTCA
ATTCCCGTCAACAPACGTTTGACCCTAATCCTTTCTTCAGAGGTAAATCAGTTTGTAGAA
TGCTGTTACAACACGTGATCCCCAGCCTGAGCTGTACGTTAACAGGTACTACTACCAAAC
GTCATGTTGGTTTTTGAACAGGACAACACTACTGCGACTTCGAGATACAGTTTGAGATGGTTC
ACAATGTTCTCCATGCTTGGCTTGGTGGAAGAGCTACTTATTCTATTTCTTCTCTTGATTA
TTCTGCATTGCAACCTGTGTTTTCTTCCACATGCGAACACAGATAGATTGTGGGCCATC
TGGCAGGAGCTGCAGAGGTACAGGAAGAAGCCATACAAATGAAGCGGATTGTGCCATTAACC
TAATGCGCAAACCTCTACATCCCTTCGACAACAGTGATCTCAATCATGATCCTGTAACCTT
TAAATACTCAAAACCCACTGATGGCTTTGACTACCAGAACAACCTTTGGATACAAGTATGAC
AACCTTGAGTTCAATCATTTTCAGTATTCCCAGGCTTGAAGCAATCATTCGATTAGACAAC
GTCAAGATCGTGTGTTTGCAGGATTCCTCCTTCACAACATTGGGACATCCGCAACTTGTGA
GATATTCGTCTGTGTCCTTACCACCAGCGGTGAGCAAACTGTGAAAACAAAGCCGGAACA
TTTGCCGTAAGTTCGGAGGAGAAACAGAGATGGCGTTTCATTTTGACAGACTCTACAGGTTTG
ACATCAGTGAACACTGAGGGACCTCGGCATACAGCTGGACAGCCATGACTTTGACCTCAG
CATCAAGATTCAAGGAGTAAATGGATCCTACCTTGATCCACACATCCTGCCAGAGCCATCC
TTGATTTTTGTGCCTGGTTCAAGT

Intron d/e

AAGAAAGTTTCACTGTCTAAATCTTTTTTTATGATAGAGGGTAGAGAAGTGGAGACAATGT
GACAATATATTGAATAAAGTTGTTTAAATTTATAACTCTCATAAGTTCATATTATGCTGA
AGCTGTAGCCATCTATAACTGTGTAACATGAAATGTTAAGACATTAACCTAATACTTCAG
CTGATAACAAAACAAATGTTAATACATACGTCAATGTAACATTTCTTATCTTTAGGTTATA
GCATAAACACTTCAGAGATACAGTGACGAAAACCTCTATTTAAATATTTTCAGGT

Domäne e

TCTTTCCCTGCGTCTGATGGGCATTTCAGATGACATCCTTGTGAGAAAAGAAGTGAACAGCC
TGACAACCAGGGAGACTGCATCTCTGATCCATGCTCTGAAAAGTATGCAGGAAGACCATTTC
ACCTGACGGGTTCCAAGCCATTGCCTCTTTCCATGCTCTGCCACCACTCTGCCCTTCACCA
TCTGCAGCTCACCGTTATGCTTGTGTGTCACGGCATGGCTACATTTCCCCAGTGGCACA
GATTGTACACTGTACAGTTCCAGGATGCACTGAGGAGACATGGAGCTACGGTAGGTGTACC
GTATTGGGATTGGCTGCGACCGCAGTCTCACCTACCAGAGCTTGTCAACCATGGAGACATAC

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CATGATATTTGGAGTAACAGAGATTTCCCCAATCCTTTCTACCAAGCCAAATATTGAGTTTG
 AAGGAGAAACATTACAAACAGAGAGAGAGAGTCAATTGCAGACAAACTTTTTGTCAAAGGTGG
 ACACGTTTTTTGATAAACTGGTTCTTCAAACAAGCCATCCTAGCGCTGAGCAGGAAAACCTAC
 TGTGACTTTGAGATTCAAGTTTGAAATTCTTCACAACGGCGTTACACAGTGGGTGGGAGGCA
 GTCGTACCTACTCTATCGGACATCTTCATTACGCATTCTACGACCCCTCTTTTCTACCTTCA
 CCATTTCCAGACAGACCGTATTTGgGCAATCTGGCAAGAAGCTCCAGGAACAGAGAGGGGCTC
 TCGGGTGATGAGGCTCACTGTGCTCTCGAGCAATGAGAGAACCATTGAAGCCTTTTCAGCT
 TCGGCGCTCCTTATAACTGGAATCAGCTCACACAGGATTTCTCCCGACCCGAGGACACCTT
 CGACTACAGGAAGTTTGGTTATGAATATGACAATTTAGAAATTCCTGGGAAATGTCAGTTGCT
 GAACTGGATCAATACATTATTGAACATCAAGAAAATGATAGAGTATTCGCTGGGTTCTCTGT
 TGAGTGGATTCCGAGGTTCCGCATCAGTTAATTTCCAGGTTTGTAGAGCTGATTCCACATG
 TCAGGATGCTGGGTACTTCACCGTTCTTGGTGGCAGTGTGAGATGGCGTGGGCATTTGAC
 AGGCTTTACAAATATGACATTACTGAAACTCTGGAGAAAATGCACCTTCGATATGATGATG
 ACTTCACAAATCTCTGTCACTCTGACCGCCAACAACGGAAGTGTCTGAGCAGCAGTCTAAT
 CCCAACACCCGAGTGTCAATATCCAGCGGGGACATC

Intron e/f

AAGTAGTAAACTGCTCAGATTGTTTTTCATAATTACTCCACTATTAAGTAAAAAGTACTAGT
 AATTCAATAGTACTGTTTACAGAGAAATGTAACACAATAGACCACAGAGTCCATTTGTTAA
 ACGCCTTTGGCTTGGTAAGTCTGAGSTTTTGGTGACTGATGGAAGCTAAAATATATTTTG
 ACAG

Domäne f(1)

GTGACATAAATACCAGGAGCATGTCACCGAACCGTGTTCCCGGTGAGCTGAGCGATCTGTC
 TGCGAGGGACCTGTCTAGTCTCAAGTCTGCTCTGCGAGACCTACAGGAGGATGATGGCCCC
 AACGGATACCAGGCTCTTGACAGCCTTCCATGGGCTACCAGCAGGCTGCCATGATAGCCGGG
 GAAATGAGAT

Intron f

ATATTTAAAGTATTTTATCTTACGCATGACCCCTGACCCCTATTATTTTTTTTATCCTATGAT
 GAAACATTTACTTAGACTGGCTTGTGAGCCCCAGGCCAAATGCACTGTAAAAATACACTGA
 CAGAGGATTAGGCATTCTTGGGAGTACTGTATAGTTAGTTGCATACATATTAGCGTTCCCT
 CACTAAACGAATCTCTGAATGCTATCAATTAAAGATCATGATGCTTTGATTGTGTCTACT
 GTATTTAAATGTTGTTAAGATTTGCAATTACAATATACACAAACACGTTTCTGCACTCTC
 GGAGAATGCAATCTTTTCGTTGTACGCGTCTGTTTTCATATTTTTATGCATGTAGTTTGCAC
 TACTTAGCGTCCAAATAAATCCATTACAAAATCACACAAACAAACGATTTTAGGAATGTGA
 CTGTAGCTGCAACGAATATACCTGATCCTTTCTTGTTCAGAT

Domäne f(2)

CGCATGTTGCATTACAGGGATGCCGACCTTCCCCAGTGGCACAGACTGTACACCCTGCAG
 TTGGAGATGGCTCTGAGGAGACATGGATCATCTGTGCGCATCCCCTACTGGGACTGGACAA
 AGCCTATCTCCGAACCTCCCTCGCTCTTCAACAGCCCTGAGTATTATGACCCATGGCATGA
 TGCTGTGGTAAACAACCCATTCTCCAAAGGTTTTGTCAAATTTGCLAATACCTACACAGTA
 AGAGACCCACAGGAGATGCTGTTCCAGCTTTGTGAACATGGAGAGTCAATCCTCTATGAGC
 AAATCTCTTCTTGCTCTTGAGCAAACCGACTACTGTGATTTTGGAGGTACAGTTTGGAGTCT
 CCATAACGTGATCCACTACCTTGTGTTGGTGGAGCTCAGACCTACGCATTGTCTTCTCTGCAT
 TATGCCCTCCTACGACCCATTCTTCTTTATACACCATTCCTTTGTGGATAAGATGTGGGTAG
 TATGGCAAGCTCTTCAAAAGAGGAGGAACCTTCCATACAAAGCGAGCTGACTGTgCTGTCAA
 CCTAATGACTAAACCAATGAGGCCATTTGACTCCGATATGAATCAGAACCCATTACAAAG
 ATGCACGCAGTTCCCAACACACTCTATGACTACGAGACACTGTACTACAGCTACGATAATC
 TCGAAATAGGTGGCAGGAATCTCGACCAGCTTCAGGCTGAAATTGACAGAAGCAGAAGCCA

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CGATCGCGTTTTTGGCTGGATTCTTGCTTCGTGGAATCGGAACTTCTGCTGATGTCAGGTTT
 TGGATTTGTAGAAATGAAATGACTGCCACAGGGGTGGAATAATTTTCATCTTAGGTGGAG
 CCAAGGAAATGCCATGGTCATTTGACAGAACTTCAAGTTTGATATCACCCATGTACTCGA
 GAATGCTGGCATTAGCCCAGAGGACGTGTTTGATGCTGAGGAGCCATTTTATATCAAGGTT
 GAGATCCATGCTGTTAACAAGACCATGATACCGTCGTCTGTGATCCCAGCCCCAACTATCA
 TCTATTCTCCTGGGGAAG

Intron f/g

GTGAGAGAACCAGTAATAGCTACTGTCTACAAAGAATGTGTTTCATTTAAAGACCTGACTGT
 AGGCCGATGGCTGCTGTCTATCTCCTCCGCCTCCTCCTCCTGTTCCCTCCTCCGAAGGGGTCA
 GCTTCAGGTTCTCTTGCCAATATGCCAAGCAGACCTCCTGAGCAGGCAGTATATATACGTA
 AGGGGAGCAAGTATGGACCATCGCGCGGCATGTAGAGATACAATGATCAGCTGTCTGCTGT
 TCCACTCCTGTGACACAATGAGATAAACATGAATACAGTATTACTCAGCAGCGTTTCCAATT
 TTTAAGCCCTCGTATTTATTAAAAAAGGAATTTTAAATATATTTTTCTCCTTGTTGAAATA
 TTTTAGTAACGTGTTAATCGATATAGAGTGGAGTAGTGACGCTTTATTTTCGGTTCATTCTCG
 AAACAAAAATATAATAGTCCACTGAACTCTCTTAAATTGTTTTTACAACCTTCAACTGCCA
 CAGACGTAATCCCTCACGTTATTTTGAGCTGACAACGTGTTGAATTGAGTGTGTTCCGAAT
 TCTAATAAGCATGTATATATTTACGTCTCATGCAAGTAATATATGTTTTACTGATGACGT
 CACTTGGGTGACCACTGATTTAGTTCCTTTGTGATAATTGCAGTTTCTGTTGTACGGGGAC
 GGTGGGGGAGCCAGGTTCCCTCCTGTGACGCTGAATATCCCGTTTGAATCCCCCACATGGGT
 ACAAGTGTGATGCCTATTTCTGGTGTCCCCACCGTGATATTGCTGGAATAAGTGGCTTA
 ATACCATATACACTCACTCTATTGTACACTACTGCCACCGGCTCACACCTCTGATGCTTC
 TGTTCATCCAG

Domäne g(1)

GTCGCGCTGCTGACAGTGCGCACTCTGCCAACATTGCTGGCTCTGGGGTGAGGAAGGACGT
 CACGACCCTCACTGTGTCTGAGACCGAGAACCTAAGACAGGCTCTTCAAGGTGTCTATCGAT
 GATACTGGTCCCAATGGTTACCAAGCAATAGCATCCTTCCACGGAAGTCCCTCCAATGTGCG
 AGATGAACGGCCGCAAGGTTGCCTGTTGTGCTCACG

Intron g(1)

GTAATTAATGGATGTGAAGTCAATGTCCGAGGGTATAATAAGGATTTAAATACTTCAGTCG
 TGTAATACTGTATGACATGTGTATTGGATGGTGTAGGTATTACAGGTTATAAGGCCAGTGT
 GTGTTGGGACGGTTACTTTCCCTGCACTAGTAATAAGCATTGTATTTAGCTAGCTTTTATCA
 TATAACTTTAGTTTTAGGTTTTGCGCAATTGAAATCGAAATTTTCTTTTCATTTCAAGGTTA
 TCGCACTCGTGTGTNAGAAATAGTTACTATGCTGCATTGAGAATAACACTATAGTAATAAAG
 CATATCATACAGTAAGAATAACACTATAGTAATAAAGTATATCATNCAGTAAGAATGTCAT
 TGTATGATAAATAGGTTATCACACTCGTGTGTTTTAGARTGGTTACTATCCCAGGAATAAC
 CACTATGTATTACATGTATATTGGGCAGTGTAAGTAGTAGCATTGTATATTAAATCAGTAT
 ATCGTGCTTCAAAACACCAGGATATATGGGGTATACAGTGGGCAGTGTAAGTAGCAACATT
 GTATATTAAATCAGTATATCGTACTTCAAAACACCAGGATTATGGGGTATACAGTGGGCAG
 TGTAAAGTAGTAGCATTGTATATTAAATCAGTATATCGTACTTCAAAACACCAGGATATAAT
 TCAGTATATCGTGCTTCAAAACACCAGGATATAATTCAGTATATCGTGCTTCAAAACACCA
 GGATATATGGGATATACAGTGCGGGTTTGCATACAACCTCCACCCTTTACAG

Domäne g(2)

GTATGGCCTCCTTCCACACTGGCACAGACTGTATGTGAAGCAGATGGAAGATGCCCTGGC
 TGACCACGGGTACATATCGGCATCCCTTACTGGGACTGGACAACCTGCCTTCACAGAGTTA
 CCGGCCCTTGTACAGACTCCGAGAACAATCCCTTCCATGAG

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Intron g(2)

GTCAGTTT TAGTCTCCTGTCTGAGCTAACGATACCAATTTCTCTATTTTCGAGAACCACGATG
 ACGAGAAAACAAGCAATATAGATATAGATGCAGTATAGATCAAGTTAATGAATTCATTGCT
 ATATGTTTGGCTTGTAATAAACTTTAAGAAAACGAGAGCATGCACACAAATGAAACAAACAA
 TTATGTGTTTGATAGGAATATGATATATGTATTTGGGGGCTGACGTGAGCAGGGGTGAAGG
 GACAGTTTACATTGTCAGTAACACTGGGAGTATTCTTTGATCCACAATATATAGTTTCATT
 GTGTTTCAGCAGTTACAACATAACATTATATCATACATTACGTCTGTAACATGCTTCTTTTGTG
 CTCCTTTTGCCAG

Domäne g(3)

GGTCGCATTGATCATCTCGGTGTAACCACGTCACGTTCCCCCAGAGACATGCTGTTTAAAG
 ACCCAGAGCAAGGATCAGAGTCGTTCTTCTATAGACAAGTCCTCCTGGCTTTGGAGCAGAC
 TGACTACTGCCAGTTCGAAGTCCAGTTTGAGCTGACCCACAACGCCATTCACTCCTGGACA
 GGTGGACGTAGCCCTTACGGAATGTGACCCCTCGAGTTTCACAGCCTACGATCCTCTCTCT
 GGCTTCACCACTCCAACACCGACAGAATCTGGGCTGTCTGGCAAGCACTGCAGAAATACCG
 AGGACTCCCATACAACGAAGCACACTGTGAATCCAGGTTCTGAAACAGCCCTTGAGGCCA
 TTCAACGATGACATCAACCACAATCCAATCACCAAGACTAATGCCAGGCCCTATCGATTTCAT
 TTGATTATGAGAGGCTTAACTATCAGTATGACACCCTTAGCTTCCATGGTAAGAGCATCCC
 TGAACCTGAATGACCTGCTCGAGGAAAGAAAAGAGAAGAGAGAACATTTGCTGCTTCTCT
 CTTGCTGGGAATCGGTTGCAGTGCTGATGCTCTCTTTGACATCTGCCGCCCCAATGGTGACT
 GTGTCTTTGCAGGAACCTTTGCTGTGCTGGGAGGGGAGCTAGAAATGCCCTTGGTCTCGA
 CAGACTGTTCCGCTATGACATCACCAAGTGCATGAATCAGCTCCATCTCCAGTATGATTCA
 GATTTTCAGTTTCAGGGTGAAGCTTGTGGCCCAATGGCACTGAGCTTTTCATCAGACCTTC
 TCAAGTCACCAACAATTGAACATGAACCTTG

Intron g/h

GTATGTTATCTTATCATCAAATGTGTGATCAGATACTGGAGACGTTTTTCATATTAACCTTGG
 TCAGCATTAGTTGATGATTTTGGTGCGATGTTGACGACAAGGAGTCAAGCATTAAACACATT
 CAACACATCTTTAATCTGATATGAGAAGGGAATAAATTGATCCAGTATTGATGATTGAAGT
 TAGATTAAACAGTGAAAGATATACCAGTTTTGATAATCGTATAAAACAGTAGCAGAATTGTA
 TCGTGAAAACATAAATGTGGGAAGGCGAACGCCAAGCAGATTTTAGATTACGATCGTGTGCT
 AGAATAATTCAACAATAACCCAGACGTCGGAATGTGGTTGTCTATGGCAATGGTTACGATT
 AATTGCTAACATGCACGATTTACCTATTTCA

Domäne h

AGCCACAGAGGACCAGTTGAAGAAACAGAAAGTCACTCGCCAACATACTGACGGCAATGCA
 CACTTTTCATCGTAAGGAAGTTGATTCGCTGTCCCTGGATGAAGCAAACAACCTTGAAGAATG
 CCCTTTACAAGCTACAGAACGACCACAGTCTAACGGGATACGAAGCAATCTCTGGTTACCA
 TGGATACCCCAATCTGTGTCCGGAAGAGGCGATGACAAAATACCCCTGCTGCGTCCCCGG
 ATGGGCATCTTTCTTACTGGCACAGACTCTTGACCATTCAACTGGAAAGAGCTCTTGAGC
 ACAATGGTGCAGTCTGCTTGGTGTCTCTTACTGGGACTGGAACAAGGACCTGTCTGCTACTGCC
 GGCCTTCTTCTCCGACTCCAGCAACAACCAATCCCTACTTCAAGTACCACATCGCCGGTGT
 GGTCAAGACACCGTCAGAGAGCCAACTAGTCTTATATATAACCAGCCCCAAATCCATGGTT
 ATGATTATCTCTATTACCTAGCATTGACCACGCTTGAAGAAAACAATTACTGGGACTTTGA
 GGTTCAGTATGAGATCCTCCACAACGCCGTCCACTCCTGGCTTGGAGGATCCAGAAAGTAT
 TCCATGTCTACCTGGAGTATTCGGCCCTTTGACCCTGTCTTTATGATCCTTCACTCGGGTC
 TAGACAGACTTTGGATCATCTGGCAAGAACTTCAGAAGATCAGGAGAAAGCCCTACAACCT
 CGCTAAATGTGCTTATCATATGATGGAGAGCCACTGGCGCCCTTCAGCTATCCATCTATC
 AACCAGGACGAGTTCACCCGTGCCAACTCCAAGCCTTCTACAGTTTTTTGACAGCCATAAGT

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TCGGCTACCATTACGATAACCTGAATGTTAGAGGTCACAGCATCCAAGAACTCAACACAAT
CATCAATGACTTGAGAAACACAGACAGAATCTACGCAGGATTTGTTTTGTCAGGCATCGGT
ACGCTCTGCTAGTGTCAAGATCTATCTCCGAACAGATGACAATGACGAAGAAGTTGGAACCTT
TCACTGTCCTGGGAGGAGAGAGGGGAAATGCCATGGGCCTACGAGCGAGTTTTCAAGTATGA
CATCACAGAGGTTGCAGATAGACTTAAAATTAAGTTATGGGGACACCCCTTTAACTTCCGGA
ACTGGAGATCACATCCTTACGAATGGAATCGGTGGTAAACAAGAGCCTACCCAAATCCTTT
CATCATCTACAGACCTGCCAATCATGACTACGATGTTCTTGTTATCCCAAGTANGGAAGAAA
CCTTCACATCCCTCCCAAAGTTGTCGTCAAGAAAGGCACCCGCATCGAGTTCCACCCAGTC
GATGATTCAGTTACGAGACCAAGTTGTTGATCTTGGAAGCTACACTGCACTCTTCAACTGTG
TGGTACCACCGTTTCACATACCACGGATTGGAAGTGAACCACGTCTATTCTGTCAAGCCTGG
TGACTACTATGTTACTGGACCCACGAGAGACCTTTGCCAGAATGCAGATGTCAGGATTCAT
ATCCATGTTGAGGATGAGTAA

3' UTR

CGCAACAGGT

Intron UTR

GAGATAAGAAAACCCCTTCTAACAGTAATACGACACCACATTACAGCTTAAACATGATTGCCA
TCGATGTTTTTCATGTGTAGTATACGCTTTTCAGTTCTACATAATTTTTGTTTTTCAAATCAA
GTTTAGCAAATGAATCTATCACTGGAAAATAGGGTAGGGTAGCCAAGTGGTTAAAGCGGTG
ACTGATCACGCCAAAGACGAGTGTCTAACCTGCATGGGTACAAAAGTGAAGACCATTGCT
GGTGTCTACCGCCGTAATATTGTTTTTAGTATTGCTAAAACCTTATACTCACCCATGCGCTG
TAAAAGTGGAATAATAATCATATTTCAACAAAAGCACAAAACCATTTTCATTTTCATGAAAG
CCTCTTGTTTCACCTGAAAGACGCAAGAGACAATAGTTTCCTAACATTATTTTCAGACATTG
GAAATGTCCTGCACGTGTAAACCATATATCCTTTGAAATTTTTACGACTGCATCGTATACA
ATTTATGATATAAATTTAAACCTTTAT

3' UTR

TTCTTGGTCTCCACATATTCACATATCAGCACCAAATGGTTTTCGAAGGACATTGGCGTTCT
TCTCTGGCAATGCATTTCAATACAACATTGAAAATGACTTCAGCATATCAGTGTGCTTCGA
ACGTGTTCCGGAAGTACTCAAATGTGCTATGACTGAATTATTGTACATACATAACTTATTG
ATGTTCAATAAATAAATGTTGAAACGAAAAAAAAAAAAAAAAAAAAA

Figur 7

Abgeleitete Primärstruktur des HtH2

Domäne b

HRLEFVTOVEDALIRRGSPIGVPYWDWTQPMALPLGLADNATYRDPI SGDSRHNPFDHVEVA
FENGRTERHPDSRLFEQPLFGKHTRLFDSIVYAFEQEDFCDFEVQFEMTHNNIHA WIGGGE
KYSMSSLHYTAFDPIFYLRHSNTDRLWAIWQALQIRNRNPYKAHCAWSEEROPLKPF AFSS
PLNNNEKTYENSVPNTNVYDYEGLGYTYDDLNFEGGMDLGQLEEYIQRQRQRDRTFAGFFLS
HIGTSANVEIIIDHGT LHTSVGTFFAVLGGEKEMKWGFDRLYKYEITDELRLNL RADDVFS
ISVKVTDVDGSELSSSELIPSAAIIFERSH

Domäne c

IDHQDPHHDITIRKNVDNLTPEEINSLRRAMADLQSDKTAGGFQOIAAFHGEPKWCPSPDA
EKKFSCCVHGMVFPWHRLTVQGENALRKHGCLGALPYWDWTRPLSHLPDLVLVSSRTT
PMPYSTVEARNPWYSGHIDTVGVDTTRS VRQELYEAPGFGHYTGVAQVLLALEQDDFCDF
EVQFEIAHNFIHALVGGSEPYGMASLRYTTYDPIFYLRHSNTDRLWAIWQALQYRGKPYN
SANCAIASMRKPLQPFGLTDEINPDDETROHAPFVSVDYKNNFN EYDTLDFNGLSISQL
DRELSRRKSHDRVFAGFLLHGIQQSALVKFFVCKSDDDCDHYAGEFYILGDEAEMPWG YDR
LYKYEITEQLNALDLHIGDRFFIRYEAFDLHGTSLGSNIFPKPSVIHDEGA

Domäne d

GHHQADEYDEVVTAASHIRKNLKDLSKGEVESLRS AFLQLQNDGVYENIAKFHGKPGLCDD
NGRKVACCVHGMPTFPQWHRLYVLQVENALLERGS AVSVPYWDWTETFTELPSLIAEATYF
NSRQQTDFDPNPFGRKISFENAVTTTRDPQPELYVNRYYYQNVMLVFEQDNYCDFEIQFEMV
HNVLHAWLGGRATYSSISLDYSAFDPVFFLHHANTDRLWAIWQELQRYRKKPYN EADCAIN
LMRKPLHPPDNSDLNHDVPVTFKYSKPTDGF DYQNNFGYKYDNLEFNHFSIPRLSEIIRIQ
RQDRVFAGFLLHNI GTSATVLI FVCVPTTSGEQNCENKAGTFAVLGGGETEMAFHFDRLYRF
DISETLRDLGIQLDSHDFDLSIKIQGVNGSYLDPHILPEPSLIFVPGSS

Domäne e

SFLRPDGHSDDILVRKEVNSLTRETASLIHALKSMQEDHSPDG FQAIASFHALPPLCPSP
SAAHRYACCVHGMATFPQWHRLYTVQFQDALRRHGATVGVPYWDWLRPQSHLPPELVMTET
HDIWSNRDFPNPFYQANIEFE GENITTEREVIADKLFVKGGHVFDKLV LQTSHPSAEQENY
CDFEIQFEILHNGVHTWVGGSRTYSIGHLHYAFYDPLFYLRHHTQTDRIWAIWQELQEO RGL
SGDEAHCALEQMREPLKPFSGAPYNWNQLTQDFSRPEDTFDYRKFGYEYDNLEFLGMSVA
ELDQYIIIEHQENDRVFAGFLLSGFGGSASVNFQVCRADSTCQDAGYFTVLGGS AEMAWAFD
RLYKYDITETLEKMLRYDDDFTIISVSLTANNGTVLSSSLIPTPSVIFORGH

Domäne f

RDINTRSMSPNRVRRELSDL SARDLSSLSKALRDLQEDDGPNGYQALAAFHGLPAGCHDSR
GNEIACCIHGMPTFPQWHRLYTLQLEMALRRHGSSVAIPYWDWTKPISELPSLFTSPEY YD
PWHDAVVNNPFSKGFVKFANTYTVRDPQEMLFQLCENGESILYEQTLLALEQTDYCDFEVQ
FEVLHNVIIHYLVGGRTYALSSSLHYASYDFFFFIHHSFVDKMWVWQALQKRRLPYK RAD
CAVNLMTKPMRPFDSDMNQNPFTKMHAVPNTLYDYETLYYSYDNLEIGGRNL DQLQAEIDR

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SRSHDRVFAGFLLRGIGTSADVRFWICRNENDCHRGIIIFILGGAKEMPWSFDRNFKEDIT
HVLENAGISPEDVFDAAEPFYIKVEIHAVNKTMI PSSVIPAPTIIYSPGE

Domäne g

GRAADSAHSANIAGSGVRKDVTTTLTVSETENLRQALOGVIDDTGPNGYQAIASFHGSPPMC
EMNGRKVACCAHGMASFPHWHRLYVKQMEDALADHGSHIGIPYWDWTTAFTELPALVTDSE
NNPFHEGRIDHLGVTTSRSPRDMLFNDPEQGSSEFFYRQVLLALEQTDYCOFEVQFELTHN
AIHSWTGGRSPYGMSTLEFTAYDPLFWLHHSNTDRIWAVWQALQKYRGLPYNEAHCEIQVL
KQPLRPFNDNDINHNPIKTNARPIDSFDYERFNYQYDTLSFHGKSIPELNDLLEERKREER
TFAAFLLRGIGCSADVVDICRPNGDCVFACTFAVLGGELEMPWSFDRLFRYDITRVMNQL
HLQYDSDFSFRVKLVATNGTELSDDLKSPTIEHEL

Domäne h

GAHRGPVEETEVTROHTDGNAHFHRKEVDSLDEANNLKNALYKLQNDHSLTGYEAIISGY
HGYPNLCPEEGDDKIPLLRPRMGIFPYWHRLTIQLERALEHNGALLGVPYWDWNKDLSSL
PAFFSDSSNNNPYFKYHIAGVGHDTVREPTSLIYNQIQIHGYDYLYLALTTLEENNYWDF
EVQYEILHNAVHWSLGGSQKYSMTLEYSADFVFMILHSGLDRLWIIWQELQKIRRKPN
FAKCAYHMMEEPLAPFSYPSINQDEFTRANSPSTVFD SHKFGYHYDNLNVRGHSIQELNT
IINDLRNTDRIYAGFVLSGIGTSASVKIYLRTDDNDEEVGTFTVLGGEREMPWAYERVFKY
DITEVADRLKIKLWGHPLTSGTGDHILTNIGGGKQEP TQILSSSTDLPIMTTMFLLSQXGR
NLHI PPKV VVKGTRIEFHPVDDSVTRPVVDLGSYALFNCVVP PFTYHGFELNHVYSVKP
GDYYVTGPTRDLCQNADVRIHIHVEDE

Figur 8

cDNA-Sequenz in Verbindung mit Intronstruktur des KLH1

Domäne b

GGCCTACCGTACTGGGACTGGACTGAAACCCATGACACACATTCCGGGTCTGGCAGGAAACA
 AAACCTTATGTGGATTCTCATGGTGCATCCACACAAATCCTTTTCATAGTTCAGTGATTGC
 ATTTGAAGAAAATGCTCCCCACACCAAAAGACAAATAGATCAAAGACTCTTTAAACCGCT
 ACCTTTGGACACCACACAGACCTGTTCAACCAGATTTTGTATGCCTTTGAACAAGAAGATT
 ACTGTGACTTTGAAGTCCAATTTGAGATTACCCATAACACGATTACAGCTTGGACAGGAGG
 AAGCGAACATTTCTCAATGTCGTCCCTACATTACACAGCTTTCGATCCTTTGTTTTACTTT
 CACCATTCTAACGTTGATCGTCTTTGGGCGCTTTGGCAAGCCTTACAGATGAGACGGCATA
 AACCTACAGGGCCCACTGCGCCATATCTCTGGAACATATGCATCTGAAACCATTCGCCTT
 TTCATCTCCCTTAACAATAACGAAAGACTCATGCCAATGCCATGCCAACAAGATCTAC
 GACTATGAAAATGTCCTCCATTACACATACGAAGATTTAACATTTGGAGGCATCTCTCTGG
 AAACATAGAAAAGATGATCCACGAAAACCAGCAAGAAGACAGAATATATGCCGGTTTTCT
 CCTGGCTGGCATACTGACTTCAGCAAATGTTGATATCTTCATTAAAACTACCGATTCCGTG
 CAACATAAGGCTGGAACATTTGCAGTGCTCGGTGGAAGCAAGGAAATGAAGTGGGGATTTG
 ATCGCGTTTTTCAAGTTTGACATCACGCACGTTTTTGAAGATCTCGATCTCACTGCTGATGG
 CGATTTTCGAAGTTACTGTTGACATCACTGAAGTCGATGGAACCTAACTTGCATCCAGTCTT
 ATCCACATGCTTCTGTCTTCGTGAGCATGCACGTGGTAAGCTGAATAGAG

Intron b/c

GTTTTGTAATAATTATGTAGAATTCTTTACCTCAGAATAAGATGAGGTCACATGGGTTTTG
 CAAAACCTATTACGTTCGAATTAATATTAATAATACCGGACCTCCACTGGTACATATTTAT
 CTTTATAACGATAATAGCGATGATGATGATGATGATGATGATGATGATGATGATGATGATAATG
 ATGATGCCGGTATTGCACGTAATCCAGCCGACTTAGATGACACCCTAAGGGTGCAGAAAGT
 ATAACAATTAGATTGCGTTTGCATCTGTGTATGCGTGTGCTTTAAACCAAAAGTCAAAATAA
 AAGTGCAAAACCTTAGTTTATTCATTTGATAGAGCCTTTTACGATAAGAACAATGTAATAA
 ATTAGAACATAACTGAAACCTCCGAAAGAAGGCCTGTTTGTCAAGAGAGGTATCGACATGA
 TTGACTTATAAACCTGTGCTTCTATATTTTGGAACTGTCCACTTTCTTGTGTGTGTAAGT
 TAATCACATCGCACTATGGCTGCAAGACGTGTACGAGTACACTATATACTTACCTAATGAC
 CAACCACAAGGCTGGCTTTGTTAATATTGTTATTTTACAGAAATAAACACAGAATTCCAGC
 ATTTGGCTGGTGTATTTAGCAAAACACCGATATGACACTCATGTTTTATTACATTTTTTTT
 AG

Domäne c

TTAAATTTGACAAAGTGCCAAAGGAGTCTGCTTATTTCGAAAAATGTAGACCGTTTGAGCCC
 CGAGGAGATGAATGAACCTTCGTAAAGCCCTAGCCTTACTGAAAGAGGACAAAAGTGCCGGT
 GGATTTTCAGCAGCTTGGTGCATTCCATGGGGAGCCAAAATGGTGTCTAGTCCCGAAGCAT
 CTAAAAAATTTGCCTGCTGTGTTACCGCATGTCTGTGTTCCCTCACTGGCATCGACTGTT
 GACGGTTTCAGAGTGAAAATGCTTTGAGACGACATGGCTACGATGGAGCTTTGCCGTACTGG
 GATTGGACCTCTCCTCTTAATCACCTTCCCGAAGTGGCAGATCATGAGAAGTACGTGACCC
 CTGAAGATGGGGTAGAGAAGCATAACCCCTGGTTTCGATGGTCATATAGATACAGTCGACAA
 AACAAACAAGAAGTGTTCAGAAATAACTCTTCGAACAGCCTGAGTTTGGTCATTATACA
 AATATTGCAATGCCCCATAACTACATCCATGCACTTGTAGGAGGCGCTCAGCCTTATGGTAT
 GGCATCGCTTCGCTACACTGCTTTTGATCCACTATTCTACTTGCATCACTCTAATACAGAT
 CGTATATGGGCAATATGGCAGGCTTTACAGAAGTACAGAGGAAAACCGTACAAACGTTGCTA
 ACTGTGCTGTTACATCGATGAGAGAACCTTTGCAACCATTTGGCCTCTCTGCCAATATCAA
 CACAGACCATGTAACCAAGGAGCATTCAGTGCCATTCAACGTTTTTGGATTACAAGACCAAT

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TTCAATTATGAATATGACACTTTGGAATTTAACGGTCTCTCAATCTCTCAGTTGAATAAAA
AGCTCGAAGCGATAAAGAGCCAAGACAGCTTCTTTGCAGGCTTCCTGTTATCTGGTTTCAA
GAAATCATCTCTTGTTAAATTCAATATTTGCACCGATAGCAGCAACTGTCACCCCGCTGGA
GAGTTTTTACCTTCTGGGTGATGAAAACGAGATGCCATGGGCATACGATAGAGTCTTCAAT
ATGACATAACCGAAAACTCCACGATCTAAAGCTGCATGCAGAAGACCACTTCTACATTGA
CTATGAAGTATTTGACCTTAAACCAGCAAGCCTGGGAAAAGATTTGTTCAAGCAGCCTTCA
GTCATTTCATGAACCAAGAATAG

Intron c/d

GTACTTGGTTATATGTTTCGAATATTGCCGATACCTTCAATATATATACTTTATCAAAGTAA
TTGATTAATCTGAAGTAATTTTCCCTTCCAGTAGAGATTCAGTTGATACAACAAGAATTCCG
CCCTGTTGTATGTCACCTTTATTTTCATCAAACGATTGGAAGTGAGCTGTCCATGCCACAA
GGGGTCTCTGTAACCTTCTCGTATGGGGTATAGATTATATAGACGTGGCAGACCTTACGTA
TAACTAATATTTGTGTAATGTCGTTTCAG

Domäne d

GTCACCATGAAGGCGAAGTATATCAAGCTGAAGTAACTTCTGCCAACCGTATTGCAAAAAA
CATTGAAAATCTGAGCCTTGGTGAAGTCTGAGAGCTGCCTTCCTGGAAAATTGAA
AACGATGGAACTTACGAATCAATAGCTAAATTCCATGGTAGCCCTGGTTTGTGCCAGTTAA
ATGGTAACCCCATCTCTTGTGTGTCATGGCATGCCAACTTTCCCTCACTGGCACAGACT
GTACGTGGTTGTGCTTGAGAATGCCCTCCTGAAAAAAGGATCATCTGTAGCTGTTCCCTAT
TGGGACTGGACAAAACGAATCGAACATTTACCTCACCTGATTTTCAGACGCCACTTACTACA
ATTCCAGGCAACATCACTATGAGACAAAACCCATTCCATCATGGCAAAATCACACACGAGAA
TGAAACTCACTAGGGATCCCAAGGACAGCCTCTTCCATTTCAGACTACTTTTACGAGCAG
GTCCTTTACGCCTTGGAGCAGGATAACTTCTGTGATTTTCGAGATTTCAGTTGGAGATATTAC
ACAATGCATTGCATTCTTTACTTGGTGGCAAAGGTAAATATTCCATGTCAAACCTTGATTA
CGCTGCTTTTGTATCCTGTGTTCTTCCCTTCATCACGCAACGACTGACAGAATCTGGGCAATC
TGGCAAGACCTTCAGAGGTTCCGAAAACGGCCATACCGAGAAGCGAATTGCGCTATCCAAT
TGATGCACACGCCACTCCAGCCGTTTGATAAGAGCGACAACAATGACGAGGCAACGAAAAC
GCATGCCACTCCACATGATGTTTTGAATATCAAACAGCTTTGTTATGCTTACGATAAT
CTGGAACCTGAATCACTACTCGATTCCCTCAGCTTGATCACATGCTGCPAGAAAGAAAAGGC
ATGACAGAGTATTCGCTGGCTTCCTCCCTCACAAATATTGGAACATCTGCCGATGGCCATGT
ATTTGTATGTCTCCCAACTGGGGAACACACGAAGGACTGCAGTCATGAGGCTGGTATGTTT
TCCATCTTAGGCGGTCAAACGGAGATGTCCCTTTGTATTTGACAGACTTTACAAACTTGACA
TAACTAAAGCCTTGAAAAAGAACGGTGTGCACCTGCAAGGGGATTTGATCTGGAAATTGA
GATTACGGCTGTGAATGGATCTCATCTAGACAGTCATGTCATCCACTCTCCCACTATACTG
TTTGAGGGCCGGAACAG

Intron d/e

GTAACATTTTGTCACTGTAACCAACAACCTGCAGTCTATTTTGCAATTACGATAATAACAA
TTTTTGAAATATATCTTTATTAPAGCAAAGSTTTCTAGAGACAAACAGCCGGCTCTAATTA
TTTTTTCGAACCTTACGCTTGAGTAAAGATCTGCAAATGGCAACCCTACCTATACTATTAA
AATATAATGTTACATTCTGATCTGAATGTTTAAATAATCACTTCATATTCTGTTGCA

Domäne e

ATTCTGCCCCACACAGATGATGGACACACTGAACCAGTGATGATTGCAAGATATCACACA
ATTGGACAAGCCTCAACAACCTGTCAGTGGTGAAGCCCTCGAGTCCATGAAGGCCGACCA
TCATCTGATGGGTTCCAGGCAATCGCTTCCTTCCATGCTCTTCCCTCCTTTGTCCATCAC
CAGCTGCTTCAAAGAGGTTTGGCTGCTGGCTCCATGGCATGCCAACCTTCCCGCAATG

Figur 9

Abgeleitete Primärstruktur des KLH1

Domäne b

GLPYWDWTEPMTHIPGLAGNKTYVDSHGASHTNPFHSSVIAFEENAPHTKRQIDQRLFKPA
TFGHHTDLFNQILYAFEQEDYCDFEVQFEITHNTIHAWTGGSEHFSMSSLHYTAFDPLFYF
HHSNVDRLLWAVWQALQMRRHKPYRAHCAISLEHMHLPFAFSSPLNNNEKTHANAMPNKIY
DYENVLHYTYEDLTFGGISLENIEKMIHENQQEDRIYAGFLLAGIRTSANVDIFIKTDSV
QHKAGTFAVLGGSKEMKWGFDRVFKFDITHVLKDLDLTADGDFEVTVDITEVDGTKLASSL
IPHASVIREHARGKLNK

Domäne c

VKFDKVPRSRLIRKNVDRLSPEEMNELRKALALLKEDKSAGGFQQLGAFHGEPKWCPSP
SKKFACCVHGMSVFPWHRLLTVQSENALRRHGYDGAALPYWDWTSPLNHLPELADHEKYVD
PEDGVEKHNPWFDDGHIDTVDKTTTRSVQNKLFEOPEFGHYTSIAKQVLLALEQDNFCDFEI
QYEIAHNYTHALVGGAOPYGMASLRYTAFDPLFYLLHHSNTDRIWAIWQALQKYRGKPYNVA
NCAVTSMREPLQPFGLSANINTDHTVKEHSVPFNVFDYKTNFNYEYDTLEFNGLSISOLNK
KLEAIKSQDRFFAGFLLSGFKKSSLVKFNICTDSSNCHPAGEFYLLGDENEMPWAYDRVFK
YDITEKLHDLKLHAEDHFIYIDYEVFDLKPASLGKDLFKQPSVIHEPRI

Domäne d

GHHEGEVYQAEVTSANRIRKNINLSLGELESLRAAFLEIENDGTYESIAKFHSGSPGLCQL
NGNPISCCVHGMPFTFPHWRLLYVVVVENALLKKGSSVAVPYWDWTKRIEHLPHLISDATYY
NSRQHHYETNPFHHGKIETHENEITTRDPKDSLFSHDYFYEQVLYALEQDNFCDFEIQLEIL
HNAHSLLLGGKGYKYSMSNLDYAAFDPVFFLHHATTDRIWAIWQDLQRFKRKPYREANCAIQ
LMHTPLQPFDKSDNNDEATKTHATPHDGFYQNSFGYAYDNLELNHYSIPOLDHMLQERKR
HDRVFAFGLLHNIGTSADGHVFCVCLPTGEHTKDCSHEAGMFSILGGQTEMSFVFDRLYKLD
ITKALKKNGVHLQGDFFLEIEITAVNGSHLDSHVIHSPTILFEAG

Domäne e

DSAHTDDGHTEPVMIRKDITQLDKRQQLSLVKALESMKADHSSDGFQAIASFHALPPLCP
PAASKRFACCVHGMPFTFPQWHRLYTVOFQDSLKKGAVVGLPYWDWTLPR

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Figur 10

cDNA-Sequenz in Verbindung mit Intronstruktur des KLH2

Domäne b

GGCCTGCCCTACTGGGATTGGACCATGCCAATGAGTCATTTGCCAGAACTGGCTACAAGTG
 AGACCTACCTCGATCCAGTTACTGGGGAACTAATAACAACCCCTTTCCATCACGCCCAAGT
 GGCGTTTGAATAATGGTGTAAACAAGCAGGAATCCTGATGCCAAACTTTTTATGAAACCACT
 TACGGAGACCACACTTACCTCTTCGACAGCATGATCTACGCATTTGAGCAGGAAGACTTCT
 GCGACTTTGAAGTCCAATATGAGCTCACGCATAATGCAATACATGCATGGGTTGGAGGCAG
 TGAATAAGTATTCATGCTCTCTCTTCACTacacTGCTTTTGATCCTATATTTTACCTCCAT
 CACTCAAATGTTGATCGTCTCTGGGCCATTTGGCAAGCTCTTCAAATCAGGAGAGGCAAGT
 CTTACAAGGCCCACTGCGCCTCGTCTCAAGAAAGAGAACCATTAAAGCCTTTTGCATTTCAG
 TTCCCCACTGAACAACAACGAGAAAACGTACCACAACCTCTGTCCCCACTAACGTTTATGAC
 TATGTGGGAGTTTTGCACTATCGATATGATGACCTTCAGTTTGGCGGTATGACCATGTCAG
 AACTTGAGGAATATATTCACAAGCAGACACAACATGATAGAACCCTTTGCAGGATTCTTCCT
 TTCATATATTGGAACATCAGCAAGCGTAGATATCTTCATCAATCGAGAAGGTCATGATAAA
 TACAAAGTGGGAAGTTTTGTAGTACTTGGTGGATCCAAAGAAATGAAATGGGGCTTTGATA
 GAATGTACAAGTATGAGATCACTGAGGCTCTGAAGACGCTGAATGTTGCAGTGGATGATGG
 GTTCAGCATTACTGTTGAGATCACCGATGTTGATGGATCTCCCCCATCTGCAGATCTCATT
 CCACCTCCTGCTATAATCTTTGaACGTGGTCaTG

Intron 2b/c

AGGTATTTAAAAAAGTAATAAAAACCaTATTTTCGAATGCGCTTTATGAAATATCGTGTGAC
 TGGTTCTTTAGTTTACATGGAGTGTAAACAACATGCTCCATCAGTTGACATATACTGCTCAC
 ACAAGTAAGGGATATTTGATAATGATAACAAATATAATCAAAGCGGTTATACTATCAAGA
 CTTATTCACATAATTACAGGTGAAGGGAGGTGTGATCGTGTTCAGTATCAGGTTGAGGCC
 AGAGAAGTCCCAAGTTTGAGTCTTGCGAGAAGATGATGTTTAGGCATGGGGTCGAATCACCAA
 AATCACATGACTTCAATAACGGGTTGGACCACCTCGAGCGACgATGCAAGCAGTAGAGCGT
 CTACGCATGCTCCTGATAAGGCGACCAATCTGTTCCCTGGGGAATCAGtCGCCACTCCTCTT
 GTAGTGCCACGCTCATTTCTGCTACGGTCTGGGTACCTGCTATCGGgTCTTGATCCGTAT
 CCCAAGGATGTCCCACACATGTTCAAgGTGAGAGGTGCGGGAACATCGCTGGCCACGGTaA
 GGtCTGAATTTGATGCCGTTGAAAGTGAAGCTCTGACAACcTGAGCATGGtGAGCTCTGACG
 TTGTCGTCCTGAAAGATGAATcCAGCTcCaTGaCAGCGAGCAAaGGGCAGGACGTGTTGGT
 CAATGCAGTTGTCTCTGCAGTACACACCTGTCACTCGCCACTCACAAGCGTGTAGATCTGT
 ACGACCAGTCATGGAGATCCCAGCCCACATCATAACGGACCCCTATCCATACCGATCATGA
 GCCACCATAGCAGCGTCTTGATGACGTTCTCCCTGTGCGCTCGACATCCTcACACGGCCAA
 AAGGAACGTGGACTCGTCACTGAACATGACATTAGCCAACCTGGCACTTGTCCACCGCTGA
 TGTTGGCGAGACCATTCCAGTCGAGCTCTTCGGTGTCTGGCTTTTCATCGATAACACGACGT
 AAGGTCTGCGGGCGTGAAGACGGCTCTATGCAGGCGATTTTCGGATTGTCTGGGTGCTAAC
 TCTGATCCCAGGTGCCTGCTGAAGTTGATGCTGGATCTGTGTGGCATTGAGATGGCGATTC
 CTTAGGACTGTGGAGATGATGAATCGATCTTGACTTATGGTGGTGACATTAGGACGTGCGG
 TTCGTGTCTATCCTGCACTCTTCCAGTTGTTTCGGTGACGCTCTGGTACCGGCTGATTAC
 TGACTGAGAATATCCATCTGCCGTGCGACATGAGCCTGTGTTGGCCCAGCCTGAAGCATTG
 CAATCGCCAGAGACGCTCTTCAAAGTCAATTCGACGCATGGtTTTCTGTTCAAAATGACA
 GCGTAAACAGtTTTTGGtGCTTTTATGCTTCCCAAGAGCATGAAAAACACGTTCTATgGG
 TCGtGCACACCTTACATGACAAGtGtGAAAAGTGACTTGcACCCCTTGTgGtGTTCCGATG
 CACACTCTGTTTACGTACTGATGCGATTTGGCGTCTAAACATGTTTTGGGCTCTAAACATG
 TTTTCTGTCATGATTCATATACTATTTTTGTATATTCTGGCATCAAACCAACTACAGTG
 AAATATATTTCAATATCCCCTACTTTGTGTGAGTAGTATAGATCACTGCAGACAACATATA

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GACAAAtGCAgtTaCaCCGTCAACAATCCCAGTCATTAATTATGATGaCaCTTCCACACATA
GfGTcAGTgATTGTAAATTCAaCTGTACACACTTTTCCCGTGAACATTcAGGATCTATATGA
CTAAATATATAACATTAGTATACGTGCAGTTTTGTATCGCTACGACATTGTTGTAACTCTT
TGTTTAATCATTTTaACAG

Domäne c

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WO 00/55192

PCT/EP00/02410

28/29

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Figur 11

Abgeleitete Primärstruktur von KLH2

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As a below named inventor, I hereby declare:

That my residence, post office address and citizenship are as stated below next to my name.

That I verily believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural inventors are named below) of the subject matter which is claimed and for which a patent is sought on the invention entitled: **NUCLEIC ACID MOLECULE COMPRISING A NUCLEIC ACID SEQUENCE CODING FOR A HAEMOCYANIN** the specification of which (check one)

☒ is attached hereto.

☐ was filed on _____ as Application, Serial No. _____ and was amended on ____ (if applicable).

That I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

That I acknowledge the duty to disclose information known to be material to patentability of this application in accordance with Title 37, Code of Federal Regulations § 1.56(a).

That I hereby claim foreign priority benefits under Title 35, United States Code, § 119 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate on this invention having a filing date before that of the application on which priority is claimed:

Priority Claimed

☒ Yes ☐ No

☒ Yes ☐ No

☒ Yes ☐ No

United States Application(s)

[illegible]

That all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

I hereby appoint the following attorneys, with full power of substitution and revocation, to prosecute this application and to transact all business in the United States Patent and Trademark Office connected therewith and request that all correspondence and telephone calls in respect to this application be directed to: WELSH & KATZ, LTD., 120 South Riverside Plaza, 22nd Floor, Chicago, Illinois 60606-3913, Telephone No.: (312) 655-1500:

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SEQUENCE LISTING

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<210> 7

<211> 1209

<212> DNA

<213> *Haliotis tuberculata*

<400> 7

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<210> 8

<211> 1535

<212> DNA

<213> *Haliotis tuberculata*

<400> 8

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5

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<210> 9

<211> 1003

<212> DNA

<213> *Haliotis tuberculata*

<400> 9

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<210> 10

<211> 1251

<212> DNA

<213> *Haliotis tuberculata*

<400> 10

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7

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<210> 13

<211> 1248

<212> DNA

<213> *Haliotis tuberculata*

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<210> 14

<211> 1207

<212> DNA

<213> *Haliotis tuberculata*

<400> 14

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8

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<210> 15

<211> 1546

<212> DNA

<213> *Haliotis tuberculata*

<400> 15

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<210> 16

<211> 967

<212> DNA

<213> *Megathura crenulata*

<400> 16

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9

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<210> 17

<211> 1242

<212> DNA

<213> Megathura crenulata

<400> 17

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<211> 1236

<212> DNA

<213> Megathura crenulata

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11

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13

Leu Arg Gly Lys Asn Pro Asn Ala Met Asp Cys Ala His Glu Leu Ala
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His Gln Gln Leu Gln Pro Phe Asn Arg Asp Ser Asn Pro Val Gln Leu
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Thr Lys Asp His Ser Thr Pro Ala Asp Leu Phe Asp Tyr Lys Gln Leu
275 280 285

Gly Tyr Ser Tyr Asp Ser Leu Asn Leu Asn Gly Met Thr Pro Glu Gln
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325 330 335

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340 345 350

Ala Gly Asp Phe Phe Ile Leu Gly Gly Gln Ser Glu Met Pro Trp Arg
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Phe Tyr Arg Pro Phe Phe Tyr Asp Val Thr Glu Ala Val His His Leu
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<212> PRT

<213> Haliotis tuberculata

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Gln Ala Thr Val Glu Tyr His Gly Leu Pro Ala Arg Cys Pro Arg Pro
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Asp Ala Lys Val Arg Phe Ala Cys Cys Met His Gly Met Ala Ser Phe
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His Ala Leu Val Gly Gly Thr Asp Ala Tyr Gly Met Ala Ser Leu Arg
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16

Tyr Thr Ala Tyr Asp Pro Ile Phe Phe Leu His His Ser Asn Thr Asp
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Tyr Asn Thr Ala Asn Cys Ala Ile Glu Ser Met Arg Arg Pro Leu Gln
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Pro Phe Gly Leu Ser Ser Ala Ile Asn Pro Asp Arg Ile Thr Arg Glu
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His Ala Ile Pro Phe Asp Val Phe Asn Tyr Arg Asp Asn Leu His Tyr
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Val Tyr Asp Thr Leu Glu Phe Asn Gly Leu Ser Ile Ser Gln Leu Asp
 290 295 300

Arg Glu Leu Glu Lys Ile Lys Ser His Glu Arg Val Phe Ala Gly Phe
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Leu Leu Ser Gly Ile Lys Lys Ser Ala Leu Val Lys Phe Glu Val Cys
 325 330 335

Thr Pro Pro Asp Asn Cys His Lys Ala Gly Glu Phe Tyr Leu Leu Gly
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Asp Glu Asn Glu Met Ala Trp Ala Tyr Asp Arg Leu Phe Lys Tyr Asp
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Ile Thr Gln Val Leu Glu Ala Asn His Leu His Phe Tyr Asp His Leu
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Ile Ala Gln Tyr His Gly Lys Pro Gly Lys Cys Gln Leu Asn Asp His
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18

Thr Lys Pro Leu Gln Gln Leu Gly Val Lys Leu His Gly Gly Val Phe
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<213> Haliotis tuberculata

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35 40 45

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50 55 60

Ala His Arg Tyr Ala Cys Cys Val His Gly Met Ala Thr Phe Pro Gln
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Trp His Arg Leu Tyr Thr Val Gln Val Gln Asp Ala Leu Arg Arg His
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Gly Ser Leu Val Gly Ile Pro Tyr Trp Asp Trp Thr Lys Pro Val Asn
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Glu Leu Pro Glu Leu Leu Ser Ser Ala Thr Phe Tyr His Pro Ile Arg
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Gly Pro Gly Val His Thr Glu Arg His Ile Asn Thr Glu Arg Leu Phe
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His Ser Gly Asp His Asp Gly Tyr His Asn Trp Phe Phe Glu Thr Val
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Glu Ile Ala His Asn Gly Ile His Thr Trp Ile Gly Gly Ser Ala Val
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<130> PCT1153-01966

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 <213> *Haliotis tuberculata*

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3

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<211> 1260

<212> DNA

<213> *Haliotis tuberculata*

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<210> 6

<211> 1251

<212> DNA

<213> *Haliotis tuberculata*

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4

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<210> 7

<211> 1209

<212> DNA

<213> *Haliotis tuberculata*

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<211> 1535

<212> DNA

<213> *Haliotis tuberculata*

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5

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 <211> 1003
 <212> DNA
 <213> *Haliotis tuberculata*

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 <213> *Haliotis tuberculata*

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6

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<210> 11

<211> 1244

<212> DNA

<213> *Haliotis tuberculata*

<400> 11

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<213> *Haliotis tuberculata*

<400> 12

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7

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<211> 1248

<212> DNA

<213> *Haliotis tuberculata*

<400> 13

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ccaacggata	ccaggctctt	gcagccttcc	atgggctacc	agcaggctgc	catgatagcc	180
ggggaaatga	gatcgcattg	tgcattcacg	ggatgccgac	cttccccag	tggcacagac	240
tgtacaccct	gcagttggag	atggctctga	ggagacatgg	atcatctgtc	gccatcccct	300
actgggactg	gacaaagcct	atctccgaac	tcccctcgct	cttcaccagc	cctgagtatt	360
atgacccatg	gcatgatgct	gtggtaaaca	accattcttc	caaagggttt	gtcaaatttg	420
caaataccta	cacagtaaga	gaccacaggg	agatgctggt	ccagctttgt	gaacatggag	480
agtcaatcct	ctatgagcaa	actcttcttg	ctcttgagca	aaccgactac	tgtgattttg	540
aggtacagtt	tgaggctctc	cataacgtga	tccactacct	tgttggtgga	cgtcagacct	600
acgcattgtc	ttctctgcat	tatgctcctc	acgaccctat	cttctttata	caccattcct	660
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agcgagctga	ctgtgctgtc	aacctaatga	ctaaaccaat	gaggccattt	gactccgata	780
tgaatcagaa	cccattcaca	aagatgcacg	cagttcccaa	cacactctat	gactacgaga	840
cactgtacta	cagctacgat	aatctcgaaa	taggtggcag	gaatctcgac	cagcttcagg	900
ctgaaattga	cagaagcaga	agccacgatc	gcgtttttgc	tggattcttg	cttcgtggaa	960
tcggaacttc	tgtctgatgtc	aggttttgga	tttgtagaaa	tgaaaatgac	tgccacaggg	1020
gtggaataat	tttcatctta	gggtggagcca	aggaaatgcc	atgggtcattt	gacagaaact	1080
tcaagtttga	tatcaccat	gtactcgaga	atgctggcat	tagcccagag	gacgtgtttg	1140
atgctgagga	gccattttat	atcaagggtg	agatccatgc	tgtaacaag	accatgatac	1200
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<210> 14

<211> 1207

<212> DNA

<213> *Haliotis tuberculata*

<400> 14

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atgatactgg	tcccaatggg	taccaagcaa	tagcatcctt	ccacggaagt	cctccaatgt	180
gcgagatgaa	cggccgcgaag	gttgccctgtt	gtgctcacgg	tatggcctcc	ttcccacact	240
ggcacagact	gtatgtgaag	cagatggaag	atgccctggc	tgaccacggg	tcacatatcg	300
gcatccctta	ctgggactgg	acaactgcct	tcacagagtt	acccgccctt	gtcacagact	360
ccgagaacaa	tcctttccat	gagggtcgca	ttgatcatct	cggtgtaacc	acgtcacgtt	420
ccccagaga	catgctgttt	aacgacccag	agcaaggatc	agagtgcgtt	ttctatagac	480
aagtctctct	ggctttggag	cagactgact	actgccagtt	cgaagtccag	tttgagctga	540
cccacaacgc	cattcactcc	tggacaggtg	gacgtagccc	ttacggaatg	tcgaccctcg	600
agttcacagc	ctacgatcct	ctcttctggc	ttcaccactc	caacaccgac	agaatctggg	660

9

cggcataaac	cctacagggc	ccactgcgcc	atatctctgg	aacatatgca	tctgaaacca	480
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aagatctacg	actatgaaaa	tgctctccat	tacacatacg	aagatttaac	atttggaggc	600
atctctctgg	aaaacataga	aaagatgac	cacgaaaacc	agcaagaaga	cagaatatat	660
gccggttttc	tcctggctgg	catacgtact	tcagcaaagt	ttgatatact	cattaaaact	720
accgattccg	tgcaacataa	ggctggaaca	tttgcaagtgc	tcggtggaag	caaggaaatg	780
aagtggggat	ttgatcgctg	tttcaagttt	gacatcacgc	acgttttgaa	agatctcgat	840
ctcactgctg	atggcgattt	cgaagttact	gttgacatca	ctgaagtcga	tggaaactaaa	900
cttgcatcca	gtcttattcc	acatgcttct	gtcattcgtg	agcatgcacg	tggttaagctg	960
aatagag						967

<210> 17

<211> 1242

<212> DNA

<213> Megathura crenulata

<400> 17

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gtggatttca	gcagcttggt	gcattccatg	gggagccaaa	atggtgtcct	agtcccgaag	180
catctaaaaa	atttgccctgc	tgtgttcacg	gcatgtctgt	gttcctcac	tggcatcgac	240
tgttgacggg	tcagagtga	aatgctttga	gacgacatgg	ctacgatgga	gctttgccgt	300
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tcgaccctga	agatggggta	gagaagcata	acccttggtt	cgatgggtcat	atagatacac	420
tcgacaaaac	aacaacaaga	agtgttcaga	ataaactctt	cgaacagcct	gagtttggtc	480
attatacaag	cattgccaaa	caagtactgc	tagcgttgga	acaggacaat	ttctgtgact	540
ttgaaatcca	atatgagatt	gcccataact	acatccatgc	acttgttaga	ggcgctcagc	600
cttatgggtat	ggcatcgctt	cgctacactg	cttttgatcc	actattctac	ttgcatcact	660
ctaatacaga	tcgtatatgg	gcaatatggc	aggctttaca	gaagtacaga	ggaaaaccgt	720
acaacgttgc	taactgtgct	gttacatcga	tgagagaacc	tttgcaacca	tttggcctct	780
ctgccaatat	caacacagac	catgtaacca	aggagcattc	agtgccattc	aacgtttttg	840
attacaagac	caatttcaat	tatgaatatg	acactttgga	atttaacggg	ctctcaatct	900
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tgttatctgg	tttcaagaaa	tcatctcttg	ttaaattcaa	tatttgacc	gatagcagca	1020
actgtcaccc	cgctgggag	ttttaccttc	tgggtgatga	aaacgagatg	ccatgggcat	1080
acgatagagt	cttcaaatat	gacataaccg	aaaaactcca	cgatctaaag	ctgcatgcag	1140
aagaccactt	ctacattgac	tatgaagtat	ttgaccttaa	accagcaagc	ctgggaaaag	1200
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<210> 18

<211> 1236

<212> DNA

<213> Megathura crenulata

<400> 18

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aaaacgatgg	aacttacgaa	tcaatagcta	aattccatgg	tagccctggg	ttgtgccagt	180
taaatggtaa	ccccatctct	tgttggtgct	atggcatgcc	aactttccct	cactggcaca	240
gactgtacgt	ggttgctcgt	gagaatgccc	tcctgaaaaa	aggatcatct	gtagctgttc	300
cctattggga	ctggacaaaa	cgaatcgaac	atttacctca	cctgatttca	gacgccactt	360
actacaattc	caggcaacat	cactatgaga	caaaccatt	ccatcatggc	aaaatcacac	420
acgagaatga	aatcactact	agggatccca	aggacagcct	cttccattca	gactactttt	480
acgagcaggt	cctttacgcc	ttggagcagg	ataacttctg	tgatttcgag	attcagttgg	540
agatattaca	caatgcattg	cattctttac	ttgggtggcaa	aggtaaatat	tccatgtcaa	600
accttgatta	cgtgcttttt	gatcctgtgt	tcttccctca	tcacgcaacg	actgacagaa	660
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<400> 21						
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tcgaagaaca	aacttcgttg	aggcgagcta	tggcagatct	acaggacgac	aaaacatcag	120
ggggttttcca	gcgattgca	gcattccacg	gagaaccaa	atgggtgtcca	agccccgaag	180
cggagaaaaa	atttgcacgc	tgtgttcacg	gaatggtctg	tttccctcac	tggcacagat	240
tgctgacagt	tcaaggagaa	aatgctctga	ggaaacatgg	ctttactggt	ggactgccct	300

11

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actgggactg gactcgatca atgagcgccc ttccacattt tgttgetgat cctacttaca 360
atgatgctat ttccagccag gaagaagata acccatggca tcatgggtcac atagactctg 420
ttgggcatga tactacaaga gatgtgcgtg atgatcttta tcaatctcct ggtttcgggc 480
actacacaga tattgcacaa caagtccttc tggcctttga gcaggacagt ttctgtgatt 540
ttgaggtaca atttgaaatt gcccataatt tcatacatgc actgattggg ggtaacgaac 600
catacagtat gtcactcttg aggtatacta catacagatcc aatcttcttc ttgcaccact 660
ccagtacaga ccgacttttg gccatctggc aagcaatcac tagtgcgggc gcctgcaggt 720
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<210> 22
<211> 323
<212> DNA
<213> Megathura crenulata

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atatccggga cctctcagag ggagaaattg agagcatcag atctgctttc ctccaaattc 120
aaaaagaggg tatatatgaa aacattgcaa agttccatgg aaaaccagga ctttgtgaac 180
atgatggaca tcctgttgct tgttgtgtcc atggcatgcc cacctttccc cactggcaca 240
gactgtacgt tcttcagggt gagaatgcgc tcttagaacg agggctctgca gttgctgttc 300
cttactggga ctggacccta cct 323
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<210> 23
<211> 988
<212> DNA
<213> Megathura crenulata

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gctcatggag ctcatatttg cataccatac tgggattgga caagtgcgtt tagtcatctg 120
cccgccctag tgactgacca cgagaacaat cccttccacc acggccatat tgggtcatctg 180
aatgtggata catctcgatc tccaagagac atgctgttta atgatcctga acaaggctca 240
gaatcattct tctacagaca ggttctcttg actctagaac agacagactt ctgccaatth 300
gaagttcagt ttgaacttac acacaatgcc atccactctt ggactggagg acatactcca 360
tatggaatgt catcactgga atatacagca tatgatccac tcttttatct ccaccattcc 420
aacactgatc gtatctgggc catctggcag gcaactccaga aatatagagg tcttccatac 480
aacgcagctc actgcgatat ccaagttctg aaacaacctc ttaaaccatt cagecgagtcc 540
aggaatccaa acccagtcac cagagccaat tctagggccg ttgattcatt tgattatgag 600
aaattcaatt atcaatatga cacacttacc ttccacggac tttctatccc agaacttgat 660
gccatgcttc aagagagaaa gaaggaagag agaacatttg cagccttccct gttgcacgga 720
tttggcgcca gtgctgatgt ttcgtttgat gtctgcacac ctgatggtea ttgtgccttt 780
gctggaacct tcgcgttact tgggtggggag cttgagatgc cctgggtcctt tgaaagattg 840
ttcggttacg atatcacaaa ggttctcaag cagatgaatc ttcactatga ttctgagttc 900
cactttgagt tgaagattgt tggcacagat ggaacagaac tgccatcgga tcgtatcaag 960
agccctacca ttgaacacca tggaggag 988
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<210> 24
<211> 310
<212> DNA
<213> Megathura crenulata

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<400> 24
gtcacgatca cagtgaacgt cacgatggat ttttcaggaa ggaagtcggt tccctgtccc 60
tggaatgaag caatgacctt aaaaatgcac tgtacaagct gcagaatgat caggggtccca 120
atggatatga atcaatagcc gggtaccatg gctatccatt cctctgccct gaacatgggt 180
aagaccagta cgcattgctg gtccacggaa tgccgtgatt tccacattgg cacagacttc 240
atacaatcca gtttgagaga gctctcaaa aacatggttc tcatttgggt ctgccatact 300
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310

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<220>
<221> SIGNAL
<222> (1) .. (15)
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Asn	Val	Val	Arg 20	Lys	Asp	Val	Ser	His 25	Leu	Thr	Asp	Asp	Glu 30	Val	Gln
Ala	Leu	His 35	Gly	Ala	Leu	His	Asp 40	Val	Thr	Ala	Ser	Thr 45	Gly	Pro	Leu
Ser	Phe 50	Glu	Asp	Ile	Thr	Ser 55	Tyr	His	Ala	Ala	Pro 60	Ala	Ser	Cys	Asp
Tyr 65	Lys	Gly	Arg	Lys	Ile 70	Ala	Cys	Cys	Val	His 75	Gly	Met	Pro	Ser	Phe 80
Pro	Phe	Trp	His 85	Arg	Ala	Tyr	Val	Val	Gln 90	Ala	Glu	Arg	Ala	Leu 95	Leu
Ser	Lys	Arg 100	Lys	Thr	Val	Gly	Met 105	Pro	Tyr	Trp	Asp	Trp	Thr 110	Gln	Thr
Leu	Thr 115	His	Leu	Pro	Ser	Leu	Val 120	Thr	Glu	Pro	Ile 125	Tyr	Ile	Asp	Ser
Lys 130	Gly	Gly	Lys	Ala	Gln	Thr 135	Asn	Tyr	Trp	Tyr	Arg 140	Gly	Glu	Ile	Ala
Phe 145	Ile	Asn	Lys	Lys	Thr 150	Ala	Arg	Ala	Val	Asp 155	Asp	Arg	Leu	Phe	Glu 160
Lys	Val	Glu	Pro	Gly 165	His	Tyr	Thr	His	Leu 170	Met	Glu	Thr	Val	Leu 175	Asp
Ala	Leu	Glu 180	Gln	Asp	Glu	Phe	Cys	Lys 185	Phe	Glu	Ile	Gln	Phe 190	Glu	Leu
Ala	His 195	Asn	Ala	Ile	His	Tyr	Leu 200	Val	Gly	Gly	Lys	Phe 205	Glu	Tyr	Ser
Met 210	Ser	Asn	Leu	Glu	Tyr 215	Thr	Ser	Tyr	Asp	Pro	Ile 220	Phe	Phe	Leu	His
His 225	Ser	Asn	Val	Asp	Arg 230	Leu	Phe	Ala	Ile	Trp 235	Gln	Arg	Leu	Gln	Glu 240

13

Pro	His	Trp	His	Arg	Leu	Phe	Val	Thr	Gln	Val	Glu	Asp	Ala	Leu	Val	85	90	95
Arg	Arg	Gly	Ser	Pro	Ile	Gly	Val	Pro	Tyr	Trp	Asp	Trp	Thr	Lys	Pro	100	105	110
Met	Thr	His	Leu	Pro	Asp	Leu	Ala	Ser	Asn	Glu	Thr	Tyr	Val	Asp	Pro	115	120	125
Tyr	Gly	His	Thr	His	His	Asn	Pro	Phe	Phe	Asn	Ala	Asn	Ile	Ser	Phe	130	135	140
Glu	Glu	Gly	His	His	His	Thr	Ser	Arg	Met	Ile	Asp	Ser	Lys	Leu	Phe	145	150	155
Ala	Pro	Val	Ala	Phe	Gly	Glu	His	Ser	His	Leu	Phe	Asp	Gly	Ile	Leu	165	170	175
Tyr	Ala	Phe	Glu	Gln	Glu	Asp	Phe	Cys	Asp	Phe	Glu	Ile	Gln	Phe	Glu	180	185	190
Leu	Val	His	Asn	Ser	Ile	His	Ala	Trp	Ile	Gly	Gly	Ser	Glu	Asp	Tyr	195	200	205
Ser	Met	Ala	Thr	Leu	His	Tyr	Thr	Ala	Phe	Asp	Pro	Ile	Phe	Tyr	Leu	210	215	220
His	His	Ser	Asn	Val	Asp	Arg	Leu	Trp	Ala	Ile	Trp	Gln	Ala	Leu	Gln	225	230	235
Ile	Arg	Arg	His	Lys	Pro	Tyr	Gln	Ala	His	Cys	Ala	Gln	Ser	Val	Glu	245	250	255
Gln	Leu	Pro	Met	Lys	Pro	Phe	Ala	Phe	Pro	Ser	Pro	Leu	Asn	Asn	Asn	260	265	270
Glu	Lys	Thr	His	Ser	His	Ser	Val	Pro	Thr	Asp	Ile	Tyr	Asp	Tyr	Glu	275	280	285
Glu	Val	Leu	His	Tyr	Ser	Tyr	Asp	Asp	Leu	Thr	Phe	Gly	Gly	Met	Asn	290	295	300
Leu	Glu	Glu	Ile	Glu	Glu	Ala	Ile	His	Leu	Arg	Gln	Gln	His	Glu	Arg	305	310	315
Val	Phe	Ala	Gly	Phe	Leu	Leu	Ala	Gly	Ile	Gly	Thr	Ser	Ala	Leu	Val	325	330	335
Asp	Ile	Phe	Ile	Asn	Lys	Pro	Gly	Asn	Gln	Pro	Leu	Lys	Ala	Gly	Asp	340	345	350
Ile	Ala	Ile	Leu	Gly	Gly	Ala	Lys	Glu	Met	Pro	Trp	Ala	Phe	Asp	Arg	355	360	365
Leu	Tyr	Lys	Val	Glu	Ile	Thr	Asp	Ser	Leu	Lys	Thr	Leu	Ser	Leu	Asp	370	375	380

His Ala Leu Val Gly Gly Thr Asp Ala Tyr Gly Met Ala Ser Leu Arg
195 200 205

Glu Ile Ala His Asn Gly Ile His Thr Trp Ile Gly Gly Ser Ala Val
195 200 205

Thr Ser Leu Gln His Asp Asn Gly Thr Asp Gly Tyr Gln Ala Ile Ala
35 40 45

Gln Val Leu Leu Ala Leu Glu Gln Thr Asp Phe Cys Lys Phe Glu Val
165 170 175

22

Gln Phe Glu Ile Thr His Asn Ala Ile His Ser Trp Thr Gly Gly His
180 185 190

Ser Pro Tyr Gly Met Ser Thr Leu Asp Phe Thr Ala Tyr Asp Pro Leu
195 200 205

Phe Trp Leu His His Ser Asn Thr Asp Arg Ile Trp Ala Val Trp Gln
210 215 220

Ala Leu Gln Glu Tyr Arg Gly Leu Pro Tyr Asn His Ala Asn Cys Glu
225 230 235 240

Ile Gln Ala Met Lys Thr Pro Leu Arg Pro Phe Ser Asp Asp Ile Asn
245 250 255

His Asn Pro Val Thr Lys Ala Asn Ala Lys Pro Leu Asp Val Phe Glu
260 265 270

Tyr Asn Arg Leu Ser Phe Gln Tyr Asp Asn Leu Ile Phe His Gly Tyr
275 280 285

Ser Ile Pro Glu Leu Asp Arg Val Leu Glu Glu Arg Lys Glu Glu Asp
290 295 300

Arg Ile Phe Ala Ala Phe Leu Leu Ser Gly Ile Lys Arg Ser Ala Asp
305 310 315 320

Val Val Phe Asp Ile Cys Gln Pro Glu His Glu Cys Val Phe Ala Gly
325 330 335

Thr Phe Ala Ile Leu Gly Gly Glu Leu Glu Met Pro Trp Ser Phe Asp
340 345 350

Arg Leu Phe Arg Tyr Asp Ile Thr Lys Val Met Lys Gln Leu His Leu
355 360 365

Arg His Asp Ser Asp Phe Thr Phe Arg Val Lys Ile Val Gly Thr Asp
370 375 380

Asp His Glu Leu Pro Ser Asp Ser Val Lys Ala Pro Thr Ile Glu Phe
385 390 395 400

Glu Pro Gly

<210> 32

<211> 511

<212> PRT

<213> *Haliotis tuberculata*

<400> 32

Val His Arg Gly Gly Asn His Glu Asp Glu His His Asp Asp Arg Leu
1 5 10 15

Ala Asp Val Leu Ile Arg Lys Glu Val Asp Phe Leu Ser Leu Gln Glu
20 25 30


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<400> 33
His Arg Leu Phe Val Thr Gln Val Glu Asp Ala Leu Ile Arg Arg Gly
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Ser Pro Ile Gly Val Pro Tyr Trp Asp Trp Thr Gln Pro Met Ala His
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Leu Pro Gly Leu Ala Asp Asn Ala Thr Tyr Arg Asp Pro Ile Ser Gly
          35          40          45
Asp Ser Arg His Asn Pro Phe His Asp Val Glu Val Ala Phe Glu Asn
  50          55          60
Gly Arg Thr Glu Arg His Pro Asp Ser Arg Leu Phe Glu Gln Pro Leu
  65          70          75          80

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Ile Asp His Gln Asp Pro His His Asp Thr Ile Ile Arg Lys Asn Val
1 5 10 15

Gly Phe Leu Leu His Gly Ile Gln Gln Ser Ala Leu Val Lys Phe Phe
325 330 335

Val Cys Lys Ser Asp Asp Asp Cys Asp His Tyr Ala Gly Glu Phe Tyr
340 345 350

Ile Leu Gly Asp Glu Ala Glu Met Pro Trp Gly Tyr Asp Arg Leu Tyr
355 360 365

Lys Tyr Glu Ile Thr Glu Gln Leu Asn Ala Leu Asp Leu His Ile Gly
370 375 380

Asp Arg Phe Phe Ile Arg Tyr Glu Ala Phe Asp Leu His Gly Thr Ser
385 390 395 400

Leu Gly Ser Asn Ile Phe Pro Lys Pro Ser Val Ile His Asp Glu Gly
405 410 415

Ala

<210> 35

<211> 415

<212> PRT

<213> *Haliotis tuberculata*

<400> 35

Gly His His Gln Ala Asp Glu Tyr Asp Glu Val Val Thr Ala Ala Ser
1 5 10 15

His Ile Arg Lys Asn Leu Lys Asp Leu Ser Lys Gly Glu Val Glu Ser
20 25 30

Leu Arg Ser Ala Phe Leu Gln Leu Gln Asn Asp Gly Val Tyr Glu Asn
35 40 45

Ile Ala Lys Phe His Gly Lys Pro Gly Leu Cys Asp Asp Asn Gly Arg
50 55 60

Lys Val Ala Cys Cys Val His Gly Met Pro Thr Phe Pro Gln Trp His
65 70 75 80

Arg Leu Tyr Val Leu Gln Val Glu Asn Ala Leu Leu Glu Arg Gly Ser
85 90 95

Ala Val Ser Val Pro Tyr Trp Asp Trp Thr Glu Thr Phe Thr Glu Leu
100 105 110

Pro Ser Leu Ile Ala Glu Ala Thr Tyr Phe Asn Ser Arg Gln Gln Thr
115 120 125

Phe Asp Pro Asn Pro Phe Phe Arg Gly Lys Ile Ser Phe Glu Asn Ala
130 135 140

<400> 36

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Glu	Val	Asn	Ser	Leu	Thr	Thr	Arg	Glu	Thr	Ala	Ser	Leu	Ile	His	Ala
			20					25					30		
Leu	Lys	Ser	Met	Gln	Glu	Asp	His	Ser	Pro	Asp	Gly	Phe	Gln	Ala	Ile
		35					40					45			
Ala	Ser	Phe	His	Ala	Leu	Pro	Pro	Leu	Cys	Pro	Ser	Pro	Ser	Ala	Ala
	50					55					60				
His	Arg	Tyr	Ala	Cys	Cys	Val	His	Gly	Met	Ala	Thr	Phe	Pro	Gln	Trp
65					70					75					80
His	Arg	Leu	Tyr	Thr	Val	Gln	Phe	Gln	Asp	Ala	Leu	Arg	Arg	His	Gly
				85					90					95	
Ala	Thr	Val	Gly	Val	Pro	Tyr	Trp	Asp	Trp	Leu	Arg	Pro	Gln	Ser	His
			100					105					110		
Leu	Pro	Glu	Leu	Val	Thr	Met	Glu	Thr	Tyr	His	Asp	Ile	Trp	Ser	Asn
		115					120					125			
Arg	Asp	Phe	Pro	Asn	Pro	Phe	Tyr	Gln	Ala	Asn	Ile	Glu	Phe	Glu	Gly
	130					135					140				
Glu	Asn	Ile	Thr	Thr	Glu	Arg	Glu	Val	Ile	Ala	Asp	Lys	Leu	Phe	Val
145					150					155					160
Lys	Gly	Gly	His	Val	Phe	Asp	Lys	Leu	Val	Leu	Gln	Thr	Ser	His	Pro
				165					170					175	
Ser	Ala	Glu	Gln	Glu	Asn	Tyr	Cys	Asp	Phe	Glu	Ile	Gln	Phe	Glu	Ile
			180					185					190		
Leu	His	Asn	Gly	Val	His	Thr	Trp	Val	Gly	Gly	Ser	Arg	Thr	Tyr	Ser
		195					200					205			
Ile	Gly	His	Leu	His	Tyr	Ala	Phe	Tyr	Asp	Pro	Leu	Phe	Tyr	Leu	His
	210					215					220				
His	Phe	Gln	Thr	Asp	Arg	Ile	Trp	Ala	Ile	Trp	Gln	Glu	Leu	Gln	Glu
225					230					235					240
Gln	Arg	Gly	Leu	Ser	Gly	Asp	Glu	Ala	His	Cys	Ala	Leu	Glu	Gln	Met
				245					250					255	
Arg	Glu	Pro	Leu	Lys	Pro	Phe	Ser	Phe	Gly	Ala	Pro	Tyr	Asn	Trp	Asn
			260					265					270		
Gln	Leu	Thr	Gln	Asp	Phe	Ser	Arg	Pro	Glu	Asp	Thr	Phe	Asp	Tyr	Arg
		275					280					285			
Lys	Phe	Gly	Tyr	Glu	Tyr	Asp	Asn	Leu	Glu	Phe	Leu	Gly	Met	Ser	Val
	290					295					300				

```

<400> 37
Arg Asp Ile Asn Thr Arg Ser Met Ser Pro Asn Arg Val Arg Arg Glu
 1          5          10          15
Leu Ser Asp Leu Ser Ala Arg Asp Leu Ser Ser Leu Lys Ser Ala Leu
          20          25          30
Arg Asp Leu Gln Glu Asp Asp Gly Pro Asn Gly Tyr Gln Ala Leu Ala
          35          40          45
Ala Phe His Gly Leu Pro Ala Gly Cys His Asp Ser Arg Gly Asn Glu
          50          55          60
Ile Ala Cys Cys Ile His Gly Met Pro Thr Phe Pro Gln Trp His Arg
 65          70          75          80
Leu Tyr Thr Leu Gln Leu Glu Met Ala Leu Arg Arg His Gly Ser Ser
          85          90          95
Val Ala Ile Pro Tyr Trp Asp Trp Thr Lys Pro Ile Ser Glu Leu Pro
          100          105          110
Ser Leu Phe Thr Ser Pro Glu Tyr Tyr Asp Pro Trp His Asp Ala Val
          115          120          125

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31

Val	Asn	Asn	Pro	Phe	Ser	Lys	Gly	Phe	Val	Lys	Phe	Ala	Asn	Thr	Tyr	130	135	140
Thr	Val	Arg	Asp	Pro	Gln	Glu	Met	Leu	Phe	Gln	Leu	Cys	Glu	His	Gly	145	150	155
Glu	Ser	Ile	Leu	Tyr	Glu	Gln	Thr	Leu	Leu	Ala	Leu	Glu	Gln	Thr	Asp	165	170	175
Tyr	Cys	Asp	Phe	Glu	Val	Gln	Phe	Glu	Val	Leu	His	Asn	Val	Ile	His	180	185	190
Tyr	Leu	Val	Gly	Gly	Arg	Gln	Thr	Tyr	Ala	Leu	Ser	Ser	Leu	His	Tyr	195	200	205
Ala	Ser	Tyr	Asp	Pro	Phe	Phe	Phe	Ile	His	His	Ser	Phe	Val	Asp	Lys	210	215	220
Met	Trp	Val	Val	Trp	Gln	Ala	Leu	Gln	Lys	Arg	Arg	Lys	Leu	Pro	Tyr	225	230	235
Lys	Arg	Ala	Asp	Cys	Ala	Val	Asn	Leu	Met	Thr	Lys	Pro	Met	Arg	Pro	245	250	255
Phe	Asp	Ser	Asp	Met	Asn	Gln	Asn	Pro	Phe	Thr	Lys	Met	His	Ala	Val	260	265	270
Pro	Asn	Thr	Leu	Tyr	Asp	Tyr	Glu	Thr	Leu	Tyr	Tyr	Ser	Tyr	Asp	Asn	275	280	285
Leu	Glu	Ile	Gly	Gly	Arg	Asn	Leu	Asp	Gln	Leu	Gln	Ala	Glu	Ile	Asp	290	295	300
Arg	Ser	Arg	Ser	His	Asp	Arg	Val	Phe	Ala	Gly	Phe	Leu	Leu	Arg	Gly	305	310	315
Ile	Gly	Thr	Ser	Ala	Asp	Val	Arg	Phe	Trp	Ile	Cys	Arg	Asn	Glu	Asn	325	330	335
Asp	Cys	His	Arg	Gly	Gly	Ile	Ile	Phe	Ile	Leu	Gly	Gly	Ala	Lys	Glu	340	345	350
Met	Pro	Trp	Ser	Phe	Asp	Arg	Asn	Phe	Lys	Phe	Asp	Ile	Thr	His	Val	355	360	365
Leu	Glu	Asn	Ala	Gly	Ile	Ser	Pro	Glu	Asp	Val	Phe	Asp	Ala	Glu	Glu	370	375	380
Pro	Phe	Tyr	Ile	Lys	Val	Glu	Ile	His	Ala	Val	Asn	Lys	Thr	Met	Ile	385	390	395
Pro	Ser	Ser	Val	Ile	Pro	Ala	Pro	Thr	Ile	Ile	Tyr	Ser	Pro	Gly	Glu	405	410	415

```
<210> 38
<211> 402
<212> PRT
<213> Haliotis tuberculata
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<400> 38

Gly Arg Ala Ala Asp Ser Ala His Ser Ala Asn Ile Ala Gly Ser Gly
1 5 10 15

Val Arg Lys Asp Val Thr Thr Leu Thr Val Ser Glu Thr Glu Asn Leu
20 25 30

Arg Gln Ala Leu Gln Gly Val Ile Asp Asp Thr Gly Pro Asn Gly Tyr
35 40 45

Gln Ala Ile Ala Ser Phe His Gly Ser Pro Pro Met Cys Glu Met Asn
50 55 60

Gly Arg Lys Val Ala Cys Cys Ala His Gly Met Ala Ser Phe Pro His
65 70 75 80

Trp His Arg Leu Tyr Val Lys Gln Met Glu Asp Ala Leu Ala Asp His
85 90 95

Gly Ser His Ile Gly Ile Pro Tyr Trp Asp Trp Thr Thr Ala Phe Thr
100 105 110

Glu Leu Pro Ala Leu Val Thr Asp Ser Glu Asn Asn Pro Phe His Glu
115 120 125

Gly Arg Ile Asp His Leu Gly Val Thr Thr Ser Arg Ser Pro Arg Asp
130 135 140

Met Leu Phe Asn Asp Pro Glu Gln Gly Ser Glu Ser Phe Phe Tyr Arg
145 150 155 160

Gln Val Leu Leu Ala Leu Glu Gln Thr Asp Tyr Cys Gln Phe Glu Val
165 170 175

Gln Phe Glu Leu Thr His Asn Ala Ile His Ser Trp Thr Gly Gly Arg
180 185 190

Ser Pro Tyr Gly Met Ser Thr Leu Glu Phe Thr Ala Tyr Asp Pro Leu
195 200 205

Phe Trp Leu His His Ser Asn Thr Asp Arg Ile Trp Ala Val Trp Gln
210 215 220

Ala Leu Gln Lys Tyr Arg Gly Leu Pro Tyr Asn Glu Ala His Cys Glu
225 230 235 240

Ile Gln Val Leu Lys Gln Pro Leu Arg Pro Phe Asn Asp Asp Ile Asn
245 250 255

His Asn Pro Ile Thr Lys Thr Asn Ala Arg Pro Ile Asp Ser Phe Asp
260 265 270

Tyr Glu Arg Phe Asn Tyr Gln Tyr Asp Thr Leu Ser Phe His Gly Lys
 275 280 285
 Ser Ile Pro Glu Leu Asn Asp Leu Leu Glu Glu Arg Lys Arg Glu Glu
 290 295 300
 Arg Thr Phe Ala Ala Phe Leu Leu Arg Gly Ile Gly Cys Ser Ala Asp
 305 310 315 320
 Val Val Phe Asp Ile Cys Arg Pro Asn Gly Asp Cys Val Phe Ala Gly
 325 330 335
 Thr Phe Ala Val Leu Gly Gly Glu Leu Glu Met Pro Trp Ser Phe Asp
 340 345 350
 Arg Leu Phe Arg Tyr Asp Ile Thr Arg Val Met Asn Gln Leu His Leu
 355 360 365
 Gln Tyr Asp Ser Asp Phe Ser Phe Arg Val Lys Leu Val Ala Thr Asn
 370 375 380
 Gly Thr Glu Leu Ser Ser Asp Leu Leu Lys Ser Pro Thr Ile Glu His
 385 390 395 400
 Glu Leu

<210> 39
 <211> 515
 <212> PRT
 <213> *Haliotis tuberculata*

<400> 39
 Gly Ala His Arg Gly Pro Val Glu Glu Thr Glu Val Thr Arg Gln His
 1 5 10 15
 Thr Asp Gly Asn Ala His Phe His Arg Lys Glu Val Asp Ser Leu Ser
 20 25 30
 Leu Asp Glu Ala Asn Asn Leu Lys Asn Ala Leu Tyr Lys Leu Gln Asn
 35 40 45
 Asp His Ser Leu Thr Gly Tyr Glu Ala Ile Ser Gly Tyr His Gly Tyr
 50 55 60
 Pro Asn Leu Cys Pro Glu Glu Gly Asp Asp Lys Ile Pro Leu Leu Arg
 65 70 75 80
 Pro Arg Met Gly Ile Phe Pro Tyr Trp His Arg Leu Leu Thr Ile Gln
 85 90 95
 Leu Glu Arg Ala Leu Glu His Asn Gly Ala Leu Leu Gly Val Pro Tyr
 100 105 110

34

Trp	Asp	Trp	Asn	Lys	Asp	Leu	Ser	Ser	Leu	Pro	Ala	Phe	Phe	Ser	Asp	
		115					120					125				
Ser	Ser	Asn	Asn	Asn	Pro	Tyr	Phe	Lys	Tyr	His	Ile	Ala	Gly	Val	Gly	
	130					135					140					
His	Asp	Thr	Val	Arg	Glu	Pro	Thr	Ser	Leu	Ile	Tyr	Asn	Gln	Pro	Gln	
145					150					155					160	
Ile	His	Gly	Tyr	Asp	Tyr	Leu	Tyr	Tyr	Leu	Ala	Leu	Thr	Thr	Leu	Glu	
				165					170						175	
Glu	Asn	Asn	Tyr	Trp	Asp	Phe	Glu	Val	Gln	Tyr	Glu	Ile	Leu	His	Asn	
			180					185					190			
Ala	Val	His	Ser	Trp	Leu	Gly	Gly	Ser	Gln	Lys	Tyr	Ser	Met	Ser	Thr	
		195					200					205				
Leu	Glu	Tyr	Ser	Ala	Phe	Asp	Pro	Val	Phe	Met	Ile	Leu	His	Ser	Gly	
	210					215					220					
Leu	Asp	Arg	Leu	Trp	Ile	Ile	Trp	Gln	Glu	Leu	Gln	Lys	Ile	Arg	Arg	
225					230					235					240	
Lys	Pro	Tyr	Asn	Phe	Ala	Lys	Cys	Ala	Tyr	His	Met	Met	Glu	Glu	Pro	
				245					250					255		
Leu	Ala	Pro	Phe	Ser	Tyr	Pro	Ser	Ile	Asn	Gln	Asp	Glu	Phe	Thr	Arg	
			260					265					270			
Ala	Asn	Ser	Lys	Pro	Ser	Thr	Val	Phe	Asp	Ser	His	Lys	Phe	Gly	Tyr	
		275					280					285				
His	Tyr	Asp	Asn	Leu	Asn	Val	Arg	Gly	His	Ser	Ile	Gln	Glu	Leu	Asn	
	290					295					300					
Thr	Ile	Ile	Asn	Asp	Leu	Arg	Asn	Thr	Asp	Arg	Ile	Tyr	Ala	Gly	Phe	
305					310					315					320	
Val	Leu	Ser	Gly	Ile	Gly	Thr	Ser	Ala	Ser	Val	Lys	Ile	Tyr	Leu	Arg	
				325					330					335		
Thr	Asp	Asp	Asn	Asp	Glu	Glu	Val	Gly	Thr	Phe	Thr	Val	Leu	Gly	Gly	
			340					345					350			
Glu	Arg	Glu	Met	Pro	Trp	Ala	Tyr	Glu	Arg	Val	Phe	Lys	Tyr	Asp	Ile	
		355					360					365				
Thr	Glu	Val	Ala	Asp	Arg	Leu	Lys	Ile	Lys	Leu	Trp	Gly	His	Pro	Leu	
	370					375					380					
Thr	Ser	Gly	Thr	Gly	Asp	His	Ile	Leu	Thr	Asn	Gly	Ile	Gly	Gly	Lys	
385					390					395					400	
Gln	Glu	Pro	Thr	Gln	Ile	Leu	Ser	Ser	Ser	Thr	Asp	Leu	Pro	Ile	Met	
				405					410					415		

35

Thr Thr Met Phe Leu Leu Ser Gln Xaa Gly Arg Asn Leu His Ile Pro
 420 425 430

Pro Lys Val Val Val Lys Lys Gly Thr Arg Ile Glu Phe His Pro Val
 435 440 445

Asp Asp Ser Val Thr Arg Pro Val Val Asp Leu Gly Ser Tyr Thr Ala
 450 455 460

Leu Phe Asn Cys Val Val Pro Pro Phe Thr Tyr His Gly Phe Glu Leu
 465 470 475 480

Asn His Val Tyr Ser Val Lys Pro Gly Asp Tyr Tyr Val Thr Gly Pro
 485 490 495

Thr Arg Asp Leu Cys Gln Asn Ala Asp Val Arg Ile His Ile His Val
 500 505 510

Glu Asp Glu
 515

<210> 40
 <211> 322
 <212> PRT
 <213> Megathura crenulata

<400> 40
 Gly Leu Pro Tyr Trp Asp Trp Thr Glu Pro Met Thr His Ile Pro Gly
 1 5 10 15

Leu Ala Gly Asn Lys Thr Tyr Val Asp Ser His Gly Ala Ser His Thr
 20 25 30

Asn Pro Phe His Ser Ser Val Ile Ala Phe Glu Glu Asn Ala Pro His
 35 40 45

Thr Lys Arg Gln Ile Asp Gln Arg Leu Phe Lys Pro Ala Thr Phe Gly
 50 55 60

His His Thr Asp Leu Phe Asn Gln Ile Leu Tyr Ala Phe Glu Gln Glu
 65 70 75 80

Asp Tyr Cys Asp Phe Glu Val Gln Phe Glu Ile Thr His Asn Thr Ile
 85 90 95

His Ala Trp Thr Gly Gly Ser Glu His Phe Ser Met Ser Ser Leu His
 100 105 110

Tyr Thr Ala Phe Asp Pro Leu Phe Tyr Phe His His Ser Asn Val Asp
 115 120 125

Arg Leu Trp Ala Val Trp Gln Ala Leu Gln Met Arg Arg His Lys Pro
 130 135 140

Tyr Arg Ala His Cys Ala Ile Ser Leu Glu His Met His Leu Lys Pro
 145 150 155 160

Val	Lys	Phe	Asp	Lys	Val	Pro	Arg	Ser	Arg	Leu	Ile	Arg	Lys	Asn	Val
1				5					10					15	
Asp	Arg	Leu	Ser	Pro	Glu	Glu	Met	Asn	Glu	Leu	Arg	Lys	Ala	Leu	Ala
			20					25					30		
Leu	Leu	Lys	Glu	Asp	Lys	Ser	Ala	Gly	Gly	Phe	Gln	Gln	Leu	Gly	Ala
		35					40					45			
Phe	His	Gly	Glu	Pro	Lys	Trp	Cys	Pro	Ser	Pro	Glu	Ala	Ser	Lys	Lys
	50					55					60				
Phe	Ala	Cys	Cys	Val	His	Gly	Met	Ser	Val	Phe	Pro	His	Trp	His	Arg
65					70					75					80

37

Leu	Leu	Thr	Val	Gln	Ser	Glu	Asn	Ala	Leu	Arg	Arg	His	Gly	Tyr	Asp	
				85					90					95		
Gly	Ala	Leu	Pro	Tyr	Trp	Asp	Trp	Thr	Ser	Pro	Leu	Asn	His	Leu	Pro	
				100					105					110		
Glu	Leu	Ala	Asp	His	Glu	Lys	Tyr	Val	Asp	Pro	Glu	Asp	Gly	Val	Glu	
				115					120					125		
Lys	His	Asn	Pro	Trp	Phe	Asp	Gly	His	Ile	Asp	Thr	Val	Asp	Lys	Thr	
				130					135					140		
Thr	Thr	Arg	Ser	Val	Gln	Asn	Lys	Leu	Phe	Glu	Gln	Pro	Glu	Phe	Gly	
				145					150					155		
His	Tyr	Thr	Ser	Ile	Ala	Lys	Gln	Val	Leu	Leu	Ala	Leu	Glu	Gln	Asp	
				165					170					175		
Asn	Phe	Cys	Asp	Phe	Glu	Ile	Gln	Tyr	Glu	Ile	Ala	His	Asn	Tyr	Ile	
				180					185					190		
His	Ala	Leu	Val	Gly	Gly	Ala	Gln	Pro	Tyr	Gly	Met	Ala	Ser	Leu	Arg	
				195					200					205		
Tyr	Thr	Ala	Phe	Asp	Pro	Leu	Phe	Tyr	Leu	His	His	Ser	Asn	Thr	Asp	
				210					215					220		
Arg	Ile	Trp	Ala	Ile	Trp	Gln	Ala	Leu	Gln	Lys	Tyr	Arg	Gly	Lys	Pro	
				225					230					235		
Tyr	Asn	Val	Ala	Asn	Cys	Ala	Val	Thr	Ser	Met	Arg	Glu	Pro	Leu	Gln	
				245					250					255		
Pro	Phe	Gly	Leu	Ser	Ala	Asn	Ile	Asn	Thr	Asp	His	Val	Thr	Lys	Glu	
				260					265					270		
His	Ser	Val	Pro	Phe	Asn	Val	Phe	Asp	Tyr	Lys	Thr	Asn	Phe	Asn	Tyr	
				275					280					285		
Glu	Tyr	Asp	Thr	Leu	Glu	Phe	Asn	Gly	Leu	Ser	Ile	Ser	Gln	Leu	Asn	
				290					295					300		
Lys	Lys	Leu	Glu	Ala	Ile	Lys	Ser	Gln	Asp	Arg	Phe	Phe	Ala	Gly	Phe	
				305					310					315		
Leu	Leu	Ser	Gly	Phe	Lys	Lys	Ser	Ser	Leu	Val	Lys	Phe	Asn	Ile	Cys	
				325					330					335		
Thr	Asp	Ser	Ser	Asn	Cys	His	Pro	Ala	Gly	Glu	Phe	Tyr	Leu	Leu	Gly	
				340					345					350		
Asp	Glu	Asn	Glu	Met	Pro	Trp	Ala	Tyr	Asp	Arg	Val	Phe	Lys	Tyr	Asp	
				355					360					365		
Ile	Thr	Glu	Lys	Leu	His	Asp	Leu	Lys	Leu	His	Ala	Glu	Asp	His	Phe	
				370					375					380		

Trp Gln Asp Leu Gln Arg Phe Arg Lys Arg Pro Tyr Arg Glu Ala Asn
225 230 235 240

Cys	Ala	Ile	Gln	Leu	Met	His	Thr	Pro	Leu	Gln	Pro	Phe	Asp	Lys	Ser
				245					250						
Asp	Asn	Asn	Asp	Glu	Ala	Thr	Lys	Thr	His	Ala	Thr	Pro	His	Asp	Gly
				260					265						
Phe	Glu	Tyr	Gln	Asn	Ser	Phe	Gly	Tyr	Ala	Tyr	Asp	Asn	Leu	Glu	Leu
				275					280						
Asn	His	Tyr	Ser	Ile	Pro	Gln	Leu	Asp	His	Met	Leu	Gln	Glu	Arg	Lys
				290					295						
Arg	His	Asp	Arg	Val	Phe	Ala	Gly	Phe	Leu	Leu	His	Asn	Ile	Gly	Thr
305					310					315					
Ser	Ala	Asp	Gly	His	Val	Phe	Val	Cys	Leu	Pro	Thr	Gly	Glu	His	Thr
				325					330						
Lys	Asp	Cys	Ser	His	Glu	Ala	Gly	Met	Phe	Ser	Ile	Leu	Gly	Gly	Gln
				340					345						
Thr	Glu	Met	Ser	Phe	Val	Phe	Asp	Arg	Leu	Tyr	Lys	Leu	Asp	Ile	Thr
				355					360						
Lys	Ala	Leu	Lys	Lys	Asn	Gly	Val	His	Leu	Gln	Gly	Asp	Phe	Asp	Leu
				370					375						
Glu	Ile	Glu	Ile	Thr	Ala	Val	Asn	Gly	Ser	His	Leu	Asp	Ser	His	Val
385					390					395					
Ile	His	Ser	Pro	Thr	Ile	Leu	Phe	Glu	Ala	Gly					
				405					410						

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<210> 43
<211> 111
<212> PRT
<213> Megathura crenulata
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<400> 43
Asp Ser Ala His Thr Asp Asp Gly His Thr Glu Pro Val Met Ile Arg
  1          5          10          15
Lys Asp Ile Thr Gln Leu Asp Lys Arg Gln Gln Leu Ser Leu Val Lys
          20          25          30
Ala Leu Glu Ser Met Lys Ala Asp His Ser Ser Asp Gly Phe Gln Ala
          35          40          45
Ile Ala Ser Phe His Ala Leu Pro Pro Leu Cys Pro Ser Pro Ala Ala
  50          55          60
Ser Lys Arg Phe Ala Cys Cys Val His Gly Met Pro Thr Phe Pro Gln
  65          70          75          80

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Ser Tyr Ile Gly Thr Ser Ala Ser Val Asp Ile Phe Ile Asn Arg Glu
225 230 235 240

<400>	45														
Asp	Ala	Lys	Asp	Phe	Gly	His	Ser	Arg	Lys	Ile	Arg	Lys	Ala	Val	Asp
1				5					10					15	
Ser	Leu	Thr	Val	Glu	Glu	Gln	Thr	Ser	Leu	Arg	Arg	Ala	Met	Ala	Asp
			20					25					30		
Leu	Gln	Asp	Asp	Lys	Thr	Ser	Gly	Gly	Phe	Gln	Gln	Ile	Ala	Ala	Phe
		35					40					45			
His	Gly	Glu	Pro	Lys	Trp	Cys	Pro	Ser	Pro	Glu	Ala	Glu	Lys	Lys	Phe
	50					55					60				
Ala	Cys	Cys	Val	His	Gly	Met	Ala	Val	Phe	Pro	His	Trp	His	Arg	Leu
65					70					75					80
Leu	Thr	Val	Gln	Gly	Glu	Asn	Ala	Leu	Arg	Lys	His	Gly	Phe	Thr	Gly
				85					90					95	
Gly	Leu	Pro	Tyr	Trp	Asp	Trp	Thr	Arg	Ser	Met	Ser	Ala	Leu	Pro	His
			100					105					110		
Phe	Val	Ala	Asp	Pro	Thr	Tyr	Asn	Asp	Ala	Ile	Ser	Ser	Gln	Glu	Glu
		115					120					125			
Asp	Asn	Pro	Trp	His	His	Gly	His	Ile	Asp	Ser	Val	Gly	His	Asp	Thr
	130					135					140				
Thr	Arg	Asp	Val	Arg	Asp	Asp	Leu	Tyr	Gln	Ser	Pro	Gly	Phe	Gly	His
145					150					155					160
Tyr	Thr	Asp	Ile	Ala	Gln	Gln	Val	Leu	Leu	Ala	Phe	Glu	Gln	Asp	Ser
				165					170					175	

His Ile Arg Lys Asn Ile Arg Asp Leu Ser Glu Gly Glu Ile Glu Ser
20 25 30

44

Phe Ser Glu Ser Arg Asn Pro Asn Pro Val Thr Arg Ala Asn Ser Arg
180 185 190

Ala Val Asp Ser Phe Asp Tyr Glu Lys Phe Asn Tyr Gln Tyr Asp Thr
195 200 205

Leu Thr Phe His Gly Leu Ser Ile Pro Glu Leu Asp Ala Met Leu Gln
210 215 220

Glu Arg Lys Lys Glu Glu Arg Thr Phe Ala Ala Phe Leu Leu His Gly
225 230 235 240

Phe Gly Ala Ser Ala Asp Val Ser Phe Asp Val Cys Thr Pro Asp Gly
245 250 255

His Cys Ala Phe Ala Gly Thr Phe Ala Val Leu Gly Gly Glu Leu Glu
260 265 270

Met Pro Trp Ser Phe Glu Arg Leu Phe Arg Tyr Asp Ile Thr Lys Val
275 280 285

Leu Lys Gln Met Asn Leu His Tyr Asp Ser Glu Phe His Phe Glu Leu
290 295 300

Lys Ile Val Gly Thr Asp Gly Thr Glu Leu Pro Ser Asp Arg Ile Lys
305 310 315 320

Ser Pro Thr Ile Glu His His Gly Gly
325

<210> 48
<211> 103
<212> PRT
<213> Megathura crenulata

<400> 48
Gly His Asp His Ser Glu Arg His Asp Gly Phe Phe Arg Lys Glu Val
1 5 10 15

Gly Ser Leu Ser Leu Asp Glu Ala Asn Asp Leu Lys Asn Ala Leu Tyr
20 25 30

Lys Leu Gln Asn Asp Gln Gly Pro Asn Gly Tyr Glu Ser Ile Ala Gly
35 40 45

Tyr His Gly Tyr Pro Phe Leu Cys Pro Glu His Gly Glu Asp Gln Tyr
50 55 60

Ala Cys Cys Val His Gly Met Pro Val Phe Pro His Trp His Arg Leu
65 70 75 80

His Thr Ile Gln Phe Glu Arg Ala Leu Lys Glu His Gly Ser His Leu
85 90 95

Gly Leu Pro Tyr Trp Asp Trp
100

45

<210> 49
<211> 1269
<212> DNA
<213> *Haliotis tuberculata*

<400> 49
ggcttggttca gttttetactc gtcgcccttg tgggtgggggc tggagcagac aacgtcgtca 60
gaaaggacgt gagtcacctc acggatgacg aggtgcaagc tctccacggc gccctccatg 120
acgtcactgc atctacaggg cctctgagtt tcgaagacat aacatcttac catgccgcac 180
cagcgtcgtg tgactacaag ggacggaaga tcgcctgctg tgtccacggc atgccagtt 240
tccccctctg gcacagggca tatgtcgtcc aagccgagcg ggcactgttg tccaaacgga 300
agactgtcgg aatgccttac tgggactgga cgcaaacgct gactcaacta ccatctcttg 360
tgactgaacc catctacatt gacagtaaag gtggaaaggc tcaaaccaac tactggtacc 420
gcggcgagat agcgttcatc aataagaaga ctgcgcgagc tgtagatgat cgcctattcg 480
agaagggtgga gcctgggtcac tacacacatc ttatggagac tgtcctcgac gctctcgaac 540
aggacgaatt ctgtaaattt gaaatccagt tcgagttggc tcataatgct atccattact 600
tgggttggcgg taaatttgaa tattcaatgt caaacttgga atacacctcc tacgacccca 660
tcttcttctc ccaccactcc aacgttgacc gcctcttcgc catctggcag cgtcttcagg 720
aactgcgagg aaagaatccc aatgcaatgg actgtgcaca tgaactcgct caccagcaac 780
tccaaccctt caacagggac agcaatccag tcagctcac aaaggaccac tcgacacctg 840
ctgacctctt tgattacaaa caacttgat acagctacga cagcttaaac ctgaatggaa 900
tgacgccaga acagctgaaa acagaactag acgaacgcca ctccaaagaa cgtgcgtttg 960
caagcttccg actcagtggc tttggggggt ctgccaacgt tgttgtctat gcatgtgtcc 1020
ctgatgatga tccacgcagt gatgactact gcgagaaagc aggcgacttc ttcattcttg 1080
ggggtcaaag cgaaatgcgc tggagattct acagaccctt cttctatgat gtaactgaag 1140
cgggtacatca ccttgagtc ccgctaagtg gccactacta tgtgaaaaca gaactcttca 1200
gcgtgaatgg cacagcaatt tcacctgatc ttcttctca accaactgtt gcctaccgac 1260
ctgggaaag 1269

<210> 50
<211> 569
<212> DNA
<213> *Haliotis tuberculata*

<400> 50
ggtcttccgt actgggactg gacgcagcat ctgactcaac tcccagatct ggtgtcagac 60
cccttggttg tcgacccgga aggaggaaag gcccatgaca acgcatggta tcgtggaaac 120
atcaagtttg agaataagaa gactgcaaga gctgttgacg atcgcccttt cgagaagggt 180
ggaccaggag agaatacccg actctttgaa ggaattctcg atgctcttga acaggatgaa 240
ttctgcaact tcgagatcca gtttgagttg gctcacaacg ctatccacta cctgggttggc 300
ggcgcgtcac cgtactccat gtctcatctc gagttacacc ctctacgac cccctcttct 360
tcctccatca ctccaacacc ggaccgcac ttcgccatct gggaacgtct tcaggtactc 420
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46

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<210> 52

<211> 1242

<212> DNA

<213> *Haliotis tuberculata*

<400> 52

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<210> 53

<211> 1257

<212> DNA

<213> *Haliotis tuberculata*

<400> 53

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47

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<210> 54

<211> 1257

<212> DNA

<213> Megathura crenulata

<400> 54

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<210> 55

<211> 1254

<212> DNA

<213> Megathura crenulata

<400> 55

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48

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<210> 56

<211> 509

<212> DNA

<213> Megathura crenulata

<400> 56

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<210> 57

<211> 943

<212> DNA

<213> Megathura crenulata

<400> 57

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49

<210> 58

<211> 1248

<212> DNA

<213> Megathura crenulata

<400> 58

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<211> 1257

<212> DNA

<213> Megathura crenulata

<400> 59

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50

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<213> Megathura crenulata

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<211> 1251
<212> DNA
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gaacatctgt tttgttagat caaactcttt tagccttaga gcagacagat ttctgtgatt 540
ttgaggttca atttgaggtc gtccataatg ctattcacta ctgtgtgggt ggtcgacaag 600
tttatgctct ttcttctcaa cactatgctt catatgaccc agccttcttt atctactact 660
cctttgttga caaaatatgg gcagtcctggc aagctctgca aaagaagaga aagcgctcct 720
atcataaagc ggatttgtct cttaacatga tgaccaaaacc aatgcgacca tttgcacacg 780
atttcaatca caatggattc acaaaaatgc acgcagtccc caacactcta tttgactttc 840
aggacctttt ctacacgtat gacaacttag aaattgctgg catgaatgtt aatcagtttg 900
aagcggaaat caaccggcga aaaagccaaa caagagtctt tgccgggttc cttctacatg 960
gcattggaag atcagctgat gtacgatttt ggatttgcaa gacagctgac gactgccacg 1020
catctggcat gatctttatc ttaggaggtt cttaaagagat gcaactgggc tatgacagga 1080
actttaataa cgacatcacc caagctttga aggtcagtc cataccacct gaagatgtgt 1140
ttgacactga tgctcctttc ttcattaaag tggaggtcca tgggtgtaaac aagactgctc 1200
tccatcttc agctatccca gcacctacta taatctactc agctggtgaa g 1251

Ala Tyr Arg Pro Gly Lys
420

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<210> 64
<211> 511
<212> PRT
<213> Haliotis tuberculata
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<400> 64																
Val	His	Arg	Gly	Gly	Asn	His	Glu	Asp	Glu	His	His	Asp	Asp	Arg	Leu	
1				5					10					15		
Ala	Asp	Val	Leu	Ile	Arg	Lys	Glu	Val	Asp	Phe	Leu	Ser	Leu	Gln	Glu	
			20					25					30			
Ala	Asn	Ala	Ile	Lys	Asp	Ala	Leu	Tyr	Lys	Leu	Gln	Asn	Asp	Asp	Ser	
		35					40					45				
Lys	Gly	Gly	Phe	Glu	Ala	Ile	Ala	Gly	Tyr	His	Gly	Tyr	Pro	Asn	Met	
	50					55					60					
Cys	Pro	Glu	Arg	Gly	Thr	Asp	Lys	Tyr	Pro	Cys	Cys	Val	His	Gly	Met	
65					70					75					80	
Pro	Val	Phe	Pro	His	Trp	His	Arg	Leu	His	Thr	Ile	Gln	Met	Glu	Arg	
				85					90					95		
Ala	Leu	Lys	Asn	His	Gly	Ser	Pro	Met	Gly	Ile	Pro	Tyr	Trp	Asp	Trp	
			100					105					110			
Thr	Lys	Lys	Met	Ser	Ser	Leu	Pro	Ser	Phe	Phe	Gly	Asp	Ser	Ser	Asn	
		115					120					125				
Asn	Asn	Pro	Phe	Tyr	Lys	Tyr	Tyr	Ile	Arg	Gly	Val	Gln	His	Glu	Thr	
	130					135					140					
Thr	Arg	Asp	Val	Asn	Gln	Arg	Leu	Phe	Asn	Gln	Thr	Lys	Phe	Gly	Glu	
145					150					155					160	
Phe	Asp	Tyr	Leu	Tyr	Tyr	Leu	Thr	Leu	Gln	Val	Leu	Glu	Glu	Asn	Ser	
				165					170					175		
Tyr	Cys	Asp	Phe	Glu	Val	Gln	Tyr	Glu	Ile	Leu	His	Asn	Ala	Val	His	
			180					185					190			
Ser	Trp	Leu	Gly	Gly	Thr	Gly	Gln	Tyr	Ser	Met	Ser	Thr	Leu	Glu	His	
		195					200					205				
Ser	Ala	Phe	Asp	Pro	Val	Phe	Met	Ile	His	His	Ser	Ser	Leu	Asp	Arg	
	210					215					220					
Ile	Trp	Ile	Leu	Trp	Gln	Lys	Leu	Gln	Lys	Ile	Arg	Met	Lys	Pro	Tyr	
225					230					235					240	

54

Tyr	Ala	Leu	Asp	Cys	Ala	Gly	Asp	Arg	Leu	Met	Lys	Asp	Pro	Leu	His
				245					250					255	
Pro	Phe	Asn	Tyr	Glu	Thr	Val	Asn	Glu	Asp	Glu	Phe	Thr	Arg	Ile	Asn
			260					265					270		
Ser	Phe	Pro	Ser	Ile	Leu	Phe	Asp	His	Tyr	Arg	Phe	Asn	Tyr	Glu	Tyr
		275					280					285			
Asp	Asn	Met	Arg	Ile	Arg	Gly	Gln	Asp	Ile	His	Glu	Leu	Glu	Glu	Val
	290					295					300				
Ile	Gln	Glu	Leu	Arg	Asn	Lys	Asp	Arg	Ile	Phe	Ala	Gly	Phe	Val	Leu
305					310					315					320
Ser	Gly	Leu	Arg	Ile	Ser	Ala	Thr	Val	Lys	Val	Phe	Ile	His	Ser	Lys
				325					330					335	
Asn	Asp	Thr	Ser	His	Glu	Glu	Tyr	Ala	Gly	Glu	Phe	Ala	Val	Leu	Gly
			340					345					350		
Gly	Glu	Lys	Glu	Met	Pro	Trp	Ala	Tyr	Glu	Arg	Met	Leu	Lys	Leu	Asp
		355					360					365			
Ile	Ser	Asp	Ala	Val	His	Lys	Leu	His	Val	Lys	Asp	Glu	Asp	Ile	Arg
	370					375					380				
Phe	Arg	Val	Val	Val	Thr	Ala	Tyr	Asn	Gly	Asp	Val	Val	Thr	Thr	Arg
385					390					395					400
Leu	Ser	Gln	Pro	Phe	Ile	Val	His	Arg	Pro	Ala	His	Val	Ala	His	Asp
				405					410					415	
Ile	Leu	Val	Ile	Pro	Val	Gly	Ala	Gly	His	Asp	Leu	Pro	Pro	Lys	Val
			420					425					430		
Val	Val	Lys	Ser	Gly	Thr	Lys	Val	Glu	Phe	Thr	Pro	Ile	Asp	Ser	Ser
		435					440					445			
Val	Asn	Lys	Ala	Met	Val	Glu	Leu	Gly	Ser	Tyr	Thr	Ala	Met	Ala	Lys
	450					455					460				
Cys	Ile	Val	Pro	Pro	Phe	Ser	Tyr	His	Gly	Phe	Glu	Leu	Asp	Lys	Val
465					470					475					480
Tyr	Ser	Val	Asp	His	Gly	Asp	Tyr	Tyr	Ile	Ala	Ala	Gly	Thr	His	Ala
				485					490					495	
Leu	Cys	Glu	Gln	Asn	Leu	Arg	Leu	His	Ile	His	Val	Glu	His	Glu	
			500					505					510		

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<210> 65
<211> 197
<212> PRT
<213> Haliotis tuberculata
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55

<400> 65

Gly Leu Pro Tyr Trp Asp Trp Thr Gln His Leu Thr Gln Leu Pro Asp
 1 5 10 15
 Leu Val Ser Asp Pro Leu Phe Val Asp Pro Glu Gly Gly Lys Ala His
 20 25 30
 Asp Asn Ala Trp Tyr Arg Gly Asn Ile Lys Phe Glu Asn Lys Lys Thr
 35 40 45
 Ala Arg Ala Val Asp Asp Arg Leu Phe Glu Lys Val Gly Pro Gly Glu
 50 55 60
 Asn Thr Arg Leu Phe Glu Gly Ile Leu Asp Ala Leu Glu Gln Asp Glu
 65 70 75 80
 Phe Cys Asn Phe Glu Ile Gln Phe Glu Leu Ala His Asn Ala Ile His
 85 90 95
 Tyr Leu Val Gly Gly Arg His Thr Tyr Ser Met Ser His Leu Glu Tyr
 100 105 110
 Thr Ser Tyr Asp Pro Leu Phe Phe Leu His His Ser Asn Pro Asp Arg
 115 120 125
 Ile Phe Ala Ile Trp Glu Arg Leu Gln Val Leu Arg Gly Lys Asp Pro
 130 135 140
 Asn Thr Ala Asp Cys Ala His Asn Leu Ile His Glu Pro Met Glu Pro
 145 150 155 160
 Phe Arg Arg His Glu Pro Met Glu Pro Phe Arg Arg Asp Ser Asn Pro
 165 170 175
 Leu Asp Leu Thr Arg Glu Asn Ser Lys Pro Ile Asp Ser Phe Asp Tyr
 180 185 190
 Ala His Leu Gly Tyr
 195

<210> 66

<211> 415

<212> PRT

<213> *Haliotis tuberculata*

<400> 66

Val Thr Glu Ala Pro Ala Pro Ser Ser Asp Ala His Leu Ala Val Arg
 1 5 10 15
 Lys Asp Ile Asn His Leu Thr Arg Glu Glu Val Tyr Glu Leu Arg Arg
 20 25 30
 Ala Met Glu Arg Phe Gln Ala Asp Thr Ser Val Asp Gly Tyr Gln Ala
 35 40 45

56

Thr	Val	Glu	Tyr	His	Gly	Leu	Pro	Ala	Arg	Cys	Pro	Phe	Pro	Glu	Ala
	50					55					60				
Thr	Asn	Arg	Phe	Ala	Cys	Cys	Ile	His	Gly	Met	Ala	Thr	Phe	Pro	His
	65				70					75					80
Trp	His	Arg	Leu	Phe	Val	Thr	Gln	Val	Glu	Asp	Ala	Leu	Ile	Arg	Arg
				85					90					95	
Gly	Ser	Pro	Ile	Gly	Val	Pro	Tyr	Trp	Asp	Trp	Thr	Gln	Pro	Met	Ala
			100					105					110		
His	Leu	Pro	Gly	Leu	Ala	Asp	Asn	Ala	Thr	Tyr	Arg	Asp	Pro	Ile	Ser
		115					120					125			
Gly	Asp	Ser	Arg	His	Asn	Pro	Phe	His	Asp	Val	Glu	Val	Ala	Phe	Glu
	130					135					140				
Asn	Gly	Arg	Thr	Glu	Arg	His	Pro	Asp	Ser	Arg	Leu	Phe	Glu	Gln	Pro
	145				150					155					160
Leu	Phe	Gly	Lys	His	Thr	Arg	Leu	Phe	Asp	Ser	Ile	Val	Tyr	Ala	Phe
				165					170					175	
Glu	Gln	Glu	Asp	Phe	Cys	Asp	Phe	Glu	Val	Gln	Phe	Glu	Met	Thr	His
			180					185					190		
Asn	Asn	Ile	His	Ala	Trp	Ile	Gly	Gly	Gly	Glu	Lys	Tyr	Ser	Met	Ser
		195					200					205			
Ser	Leu	His	Tyr	Thr	Ala	Phe	Asp	Pro	Ile	Phe	Tyr	Leu	Arg	His	Ser
	210					215					220				
Asn	Thr	Asp	Arg	Leu	Trp	Ala	Ile	Trp	Gln	Ala	Leu	Gln	Ile	Arg	Arg
	225				230					235					240
Asn	Arg	Pro	Tyr	Lys	Ala	His	Cys	Ala	Trp	Ser	Glu	Glu	Arg	Gln	Pro
				245					250					255	
Leu	Lys	Pro	Phe	Ala	Phe	Ser	Ser	Pro	Leu	Asn	Asn	Asn	Glu	Lys	Thr
			260					265					270		
Tyr	Glu	Asn	Ser	Val	Pro	Thr	Asn	Val	Tyr	Asp	Tyr	Glu	Gly	Val	Leu
		275					280					285			
Gly	Tyr	Thr	Tyr	Asp	Asp	Leu	Asn	Phe	Gly	Gly	Met	Asp	Leu	Gly	Gln
	290					295					300				
Leu	Glu	Glu	Tyr	Ile	Gln	Arg	Gln	Arg	Gln	Arg	Asp	Arg	Thr	Phe	Ala
	305				310					315					320
Gly	Phe	Phe	Leu	Ser	His	Ile	Gly	Thr	Ser	Ala	Asn	Val	Glu	Ile	Ile
				325					330					335	
Ile	Asp	His	Gly	Thr	Leu	His	Thr	Ser	Val	Gly	Thr	Phe	Ala	Val	Leu
			340					345					350		

57

Pro Val Phe Phe Leu His His Ala Asn Thr Asp Arg Leu Trp Ala Ile
 210 215 220
 Trp Gln Glu Leu Gln Arg Tyr Arg Lys Lys Pro Tyr Asn Glu Ala Asp
 225 230 235 240
 Cys Ala Ile Asn Leu Met Arg Lys Pro Leu His Pro Phe Asp Asn Ser
 245 250 255
 Asp Leu Asn His Asp Pro Val Thr Phe Lys Tyr Ser Lys Pro Thr Asp
 260 265 270
 Gly Phe Asp Tyr Gln Asn Asn Phe Gly Tyr Lys Tyr Asp Asn Leu Glu
 275 280 285
 Phe Asn His Phe Ser Ile Pro Arg Leu Glu Glu Ile Ile Arg Ile Arg
 290 295 300
 Gln Arg Gln Asp Arg Val Phe Ala Gly Phe Leu Leu His Asn Ile Gly
 305 310 315 320
 Thr Ser Ala Thr Val Glu Ile Phe Val Cys Val Pro Thr Thr Ser Gly
 325 330 335
 Glu Gln Asn Cys Glu Asn Lys Ala Gly Thr Phe Ala Val Leu Gly Gly
 340 345 350
 Glu Thr Glu Met Ala Phe His Phe Asp Arg Leu Tyr Arg Phe Asp Ile
 355 360 365
 Ser Glu Thr Leu Arg Asp Leu Gly Ile Gln Leu Asp Ser His Asp Phe
 370 375 380
 Asp Leu Ser Ile Lys Ile Gln Gly Val Asn Gly Ser Tyr Leu Asp Pro
 385 390 395 400
 His Ile Leu Pro Glu Pro Ser Leu Ile Phe Val Pro Gly Ser
 405 410

<210> 68

<211> 419

<212> PRT

<213> *Haliotis tuberculata*

<400> 68

Ser Ser Phe Leu Arg Pro Asp Gly His Ser Asp Asp Ile Leu Val Arg
 1 5 10 15

Lys Glu Val Asn Ser Leu Thr Thr Arg Glu Thr Ala Ser Leu Ile His
 20 25 30

Ala Leu Lys Ser Met Gln Glu Asp His Ser Pro Asp Gly Phe Gln Ala
 35 40 45

60

Phe Thr Val Leu Gly Gly Ser Ala Glu Met Ala Trp Ala Phe Asp Arg
355 360 365

Leu Tyr Lys Tyr Asp Ile Thr Glu Thr Leu Glu Lys Met His Leu Arg
370 375 380

Tyr Asp Asp Asp Phe Thr Ile Ser Val Ser Leu Thr Ala Asn Asn Gly
385 390 395 400

Thr Val Leu Ser Ser Ser Leu Ile Pro Thr Pro Ser Val Ile Phe Gln
405 410 415

Arg Gly His

<210> 69

<211> 378

<212> PRT

<213> Megathura crenulata

<400> 69

Arg Tyr Gln Ala Thr Ala Glu Tyr His Gly Leu Pro Ala Arg Cys Pro
1 5 10 15

Arg Pro Asp Ala Lys Asp Arg Tyr Ala Cys Cys Val His Gly Met Pro
20 25 30

Ile Phe Pro His Trp His Arg Leu Phe Val Thr Gln Val Glu Asp Ala
35 40 45

Leu Val Gly Arg Gly Ala Thr Ile Gly Ile Pro Tyr Trp Asp Trp Thr
50 55 60

Glu Pro Met Thr His Ile Pro Gly Leu Ala Gly Asn Lys Thr Tyr Val
65 70 75 80

Asp Ser His Gly Ala Ser His Thr Asn Pro Phe His Ser Ser Val Ile
85 90 95

Ala Phe Glu Glu Asn Ala Pro His Thr Lys Arg Gln Ile Asp Gln Arg
100 105 110

Leu Phe Lys Pro Ala Thr Phe Gly His His Thr Asp Leu Phe Asn Gln
115 120 125

Ile Leu Tyr Ala Phe Glu Gln Glu Asp Tyr Cys Asp Phe Glu Val Gln
130 135 140

Phe Glu Ile Thr His Asn Thr Ile His Ala Trp Thr Gly Gly Ser Glu
145 150 155 160

His Phe Ser Met Ser Ser Leu His Tyr Thr Ala Phe Asp Pro Leu Phe
165 170 175

Tyr Phe His His Ser Asn Val Asp Arg Leu Trp Ala Val Trp Gln Ala
180 185 190

61

Leu Gln Met Arg Arg His Lys Pro Tyr Arg Ala His Cys Ala Ile Ser
195 200 205

Leu Glu His Met His Leu Lys Pro Phe Ala Phe Ser Ser Pro Leu Asn
210 215 220

Asn Asn Glu Lys Thr His Ala Asn Ala Met Pro Asn Lys Ile Tyr Asp
225 230 235 240

Tyr Glu Asn Val Leu His Tyr Thr Tyr Glu Asp Leu Thr Phe Gly Gly
245 250 255

Ile Ser Leu Glu Asn Ile Glu Lys Met Ile His Glu Asn Gln Gln Glu
260 265 270

Asp Arg Ile Tyr Ala Gly Phe Leu Leu Ala Gly Ile Arg Thr Ser Ala
275 280 285

Asn Val Asp Ile Phe Ile Lys Thr Thr Asp Ser Val Gln His Lys Ala
290 295 300

Gly Thr Phe Ala Val Leu Gly Gly Ser Lys Glu Met Lys Trp Gly Phe
305 310 315 320

Asp Arg Val Phe Lys Phe Asp Ile Thr His Val Leu Lys Asp Leu Asp
325 330 335

Leu Thr Ala Asp Gly Asp Phe Glu Val Thr Val Asp Ile Thr Glu Val
340 345 350

Asp Gly Thr Lys Leu Ala Ser Ser Leu Ile Pro His Ala Ser Val Ile
355 360 365

Arg Glu His Ala Arg Gly Lys Leu Asn Arg
370 375

<210> 70
<211> 419
<212> PRT
<213> Megathura crenulata

<400> 70
Asp Ser Ala His Thr Asp Asp Gly His Thr Glu Pro Val Met Ile Arg
1 5 10 15

Lys Asp Ile Thr Gln Leu Asp Lys Arg Gln Gln Leu Ser Leu Val Lys
20 25 30

Ala Leu Glu Ser Met Lys Ala Asp His Ser Ser Asp Gly Phe Gln Ala
35 40 45

Ile Ala Ser Phe His Ala Leu Pro Pro Leu Cys Pro Ser Pro Ala Ala
50 55 60

62

Ser 65	Lys	Arg	Phe	Ala	Cys 70	Cys	Val	His	Gly	Met 75	Ala	Thr	Phe	Pro	Gln 80
Trp	His	Arg	Leu	Tyr 85	Thr	Val	Gln	Phe	Gln 90	Asp	Ser	Leu	Arg	Lys 95	His
Gly	Ala	Val	Val 100	Gly	Leu	Pro	Tyr	Trp 105	Asp	Trp	Thr	Leu	Pro 110	Arg	Ser
Glu	Leu	Pro 115	Glu	Leu	Leu	Thr	Val 120	Ser	Thr	Ile	His	Asp 125	Pro	Glu	Thr
Gly	Arg 130	Asp	Ile	Pro	Asn	Pro 135	Phe	Ile	Gly	Ser	Lys 140	Ile	Glu	Phe	Glu
Gly 145	Glu	Asn	Val	His	Thr 150	Lys	Arg	Asp	Ile	Asn 155	Arg	Asp	Arg	Leu	Phe 160
Gln	Gly	Ser	Thr	Lys 165	Thr	His	His	Asn	Trp 170	Phe	Ile	Glu	Gln	Ala 175	Leu
Leu	Ala	Leu	Glu 180	Gln	Thr	Asn	Tyr	Cys 185	Asp	Phe	Glu	Val	Gln 190	Phe	Glu
Ile	Met 195	His	Asn	Gly	Val	His	Thr 200	Trp	Val	Gly	Gly	Lys 205	Glu	Pro	Tyr
Gly	Ile 210	Gly	His	Leu	His	Tyr 215	Ala	Ser	Tyr	Asp	Pro 220	Leu	Phe	Tyr	Ile
His 225	His	Ser	Gln	Thr	Asp 230	Arg	Ile	Trp	Ala	Ile 235	Trp	Gln	Ser	Leu	Gln 240
Arg	Phe	Arg	Gly	Leu 245	Ser	Gly	Ser	Glu	Ala 250	Asn	Cys	Ala	Val	Asn 255	Leu
Met	Lys	Thr 260	Pro	Leu	Lys	Pro	Phe	Ser 265	Phe	Gly	Ala	Pro	Tyr 270	Asn	Leu
Asn	Asp 275	His	Thr	His	Asp	Phe	Ser 280	Lys	Pro	Glu	Asp	Thr 285	Phe	Asp	Tyr
Gln	Lys 290	Phe	Gly	Tyr	Ile	Tyr 295	Asp	Thr	Leu	Glu	Phe 300	Ala	Gly	Trp	Ser
Ile 305	Arg	Gly	Ile	Asp	His 310	Ile	Val	Arg	Asn	Arg 315	Gln	Glu	His	Ser	Arg 320
Val	Phe	Ala	Gly	Phe 325	Leu	Leu	Glu	Gly	Phe 330	Gly	Thr	Ser	Ala	Thr 335	Val
Asp	Phe	Gln 340	Val	Cys	Arg	Thr	Ala	Gly 345	Asp	Cys	Glu	Asp	Ala 350	Gly	Tyr
Phe	Thr 355	Val	Leu	Gly	Gly	Glu	Lys 360	Glu	Met	Pro	Trp	Ala 365	Phe	Asp	Arg

<400> 74															
Gly 1	Leu	Pro	Tyr	Trp 5	Asp	Trp	Thr	Met	Pro 10	Met	Ser	His	Leu	Pro 15	Glu
Leu	Ala	Thr	Ser 20	Glu	Thr	Tyr	Leu	Asp 25	Pro	Val	Thr	Gly	Glu 30	Thr	Lys
Asn	Asn	Pro 35	Phe	His	His	Ala	Gln 40	Val	Ala	Phe	Glu	Asn 45	Gly	Val	Thr
Ser	Arg 50	Asn	Pro	Asp	Ala	Lys 55	Leu	Phe	Met	Lys	Pro 60	Thr	Tyr	Gly	Asp
His 65	Thr	Tyr	Leu	Phe	Asp 70	Ser	Met	Ile	Tyr	Ala 75	Phe	Glu	Gln	Glu	Asp 80
Phe	Cys	Asp	Phe	Glu 85	Val	Gln	Tyr	Glu	Leu 90	Thr	His	Asn	Ala	Ile 95	His
Ala	Trp	Val	Gly 100	Gly	Ser	Glu	Lys	Tyr 105	Ser	Met	Ser	Ser	Leu 110	His	Tyr
Thr	Ala	Phe 115	Asp	Pro	Ile	Phe	Tyr 120	Leu	His	His	Ser	Asn 125	Val	Asp	Arg
Leu 130	Trp	Ala	Ile	Trp	Gln	Ala 135	Leu	Gln	Ile	Arg	Arg 140	Gly	Lys	Ser	Tyr
Lys 145	Ala	His	Cys	Ala	Ser 150	Ser	Gln	Glu	Arg	Glu 155	Pro	Leu	Lys	Pro	Phe 160
Ala	Phe	Ser	Ser	Pro 165	Leu	Asn	Asn	Asn	Glu 170	Lys	Thr	Tyr	His 175	Asn	Ser
Val	Pro	Thr	Asn 180	Val	Tyr	Asp	Tyr	Val	Gly 185	Val	Leu	His 190	Tyr	Arg	Tyr

67

Asp Asp Leu Gln Phe Gly Gly Met Thr Met Ser Glu Leu Glu Glu Tyr
195 200 205

Ile His Lys Gln Thr Gln His Asp Arg Thr Phe Ala Gly Phe Phe Leu
210 215 220

Ser Tyr Ile Gly Thr Ser Ala Ser Val Asp Ile Phe Ile Asn Arg Glu
225 230 235 240

Gly His Asp Lys Tyr Lys Val Gly Ser Phe Val Val Leu Gly Gly Ser
245 250 255

Lys Glu Met Lys Trp Gly Phe Asp Arg Met Tyr Lys Tyr Glu Ile Thr
260 265 270

Glu Ala Leu Lys Thr Leu Asn Val Ala Val Asp Asp Gly Phe Ser Ile
275 280 285

Thr Val Glu Ile Thr Asp Val Asp Gly Ser Pro Pro Ser Ala Asp Leu
290 295 300

Ile Pro Pro Pro Ala Ile Ile Phe Glu Arg
305 310

<210> 75

<211> 416

<212> PRT

<213> Megathura crenulata

<400> 75

Ala Asp Ala Lys Asp Phe Gly His Ser Arg Lys Ile Arg Lys Ala Val
1 5 10 15

Asp Ser Leu Thr Val Glu Glu Gln Thr Ser Leu Arg Arg Ala Met Ala
20 25 30

Asp Leu Gln Asp Asp Lys Thr Ser Gly Gly Phe Gln Gln Ile Ala Ala
35 40 45

Phe His Gly Glu Pro Lys Trp Cys Pro Ser Pro Glu Ala Glu Lys Lys
50 55 60

Phe Ala Cys Cys Val His Gly Met Ala Val Phe Pro His Trp His Arg
65 70 75 80

Leu Leu Thr Val Gln Gly Glu Asn Ala Leu Arg Lys His Gly Phe Thr
85 90 95

Gly Gly Leu Pro Tyr Trp Asp Trp Thr Arg Ser Met Ser Ala Leu Pro
100 105 110

His Phe Val Ala Asp Pro Thr Tyr Asn Asp Ala Ile Ser Ser Gln Glu
115 120 125

Glu Asp Asn Pro Trp His His Gly His Ile Asp Ser Val Gly His Asp
130 135 140

<210>	76
<211>	419
<212>	PRT

<213> Megathura crenulata

<400> 76

Gly Ser His Gln Ala Asp Glu Tyr Arg Glu Ala Val Thr Ser Ala Ser
1 5 10 15

His Ile Arg Lys Asn Ile Arg Asp Leu Ser Glu Gly Glu Ile Glu Ser
20 25 30

Ile Arg Ser Ala Phe Leu Gln Ile Gln Lys Glu Gly Ile Tyr Glu Asn
35 40 45

Ile Ala Lys Phe His Gly Lys Pro Gly Leu Cys Glu His Asp Gly His
50 55 60

Pro Val Ala Cys Cys Val His Gly Met Pro Thr Phe Pro His Trp His
65 70 75 80

Arg Leu Tyr Val Leu Gln Val Glu Asn Ala Leu Leu Glu Arg Gly Ser
85 90 95

Ala Val Ala Val Pro Tyr Trp Asp Trp Thr Glu Lys Ala Asp Ser Leu
100 105 110

Pro Ser Leu Ile Asn Asp Ala Thr Tyr Phe Asn Ser Arg Ser Gln Thr
115 120 125

Phe Asp Pro Asn Pro Phe Phe Arg Gly His Ile Ala Phe Glu Asn Ala
130 135 140

Val	Thr	Ser	Arg	Asp	Pro	Gln	Pro	Glu	Leu	Trp	Asp	Asn	Lys	Asp	Phe
145					150					155					160

Tyr Glu Asn Val Met Leu Ala Leu Glu Gln Asp Asn Phe Cys Asp Phe
165 170 175

Glu Ile Gln Leu Glu Leu Ile His Asn Ala Leu His Ser Arg Leu Gly
180 185 190

Gly Arg Ala Lys Tyr Ser Leu Ser Ser Leu Asp Tyr Thr Ala Phe Asp
195 200 205

Pro Val Phe Phe Leu His His Ala Asn Val Asp Arg Ile Trp Ala Ile
210 215 220

Trp Gln Asp Leu Gln Arg Tyr Arg Lys Lys Pro Tyr Asn Glu Ala Asp
225 230 235 240

Cys Ala Val Asn Glu Met Arg Lys Pro Leu Gln Pro Phe Asn Asn Pro
245 250 255

Glu Leu Asn Ser Asp Ser Met Thr Leu Lys His Asn Leu Pro Gln Asp
260 265 270

Ser Phe Asp Tyr Gln Asn Arg Phe Arg Tyr Gln Tyr Asp Asn Leu Gln
275 280 285

Asp 1	Gly	Leu	Ser	Gln 5	His	Asn	Leu	Val	Arg 10	Lys	Glu	Val	Ser	Ser 15	Leu
Thr	Thr	Leu	Glu 20	Lys	His	Phe	Leu	Arg 25	Lys	Ala	Leu	Lys	Asn 30	Met	Gln
Ala	Asp	Asp 35	Ser	Pro	Asp	Gly	Tyr 40	Gln	Ala	Ile	Ala	Ser 45	Phe	His	Ala
Leu	Pro 50	Pro	Leu	Cys	Pro	Ser 55	Pro	Ser	Ala	Ala	His 60	Arg	His	Ala	Cys
Cys 65	Leu	His	Gly	Met	Ala 70	Thr	Phe	Pro	Gln	Trp 75	His	Arg	Leu	Tyr	Thr 80
Val	Gln	Phe	Glu	Asp 85	Ser	Leu	Lys	Arg 90	His	Gly	Ser	Ile	Val	Gly 95	Leu
Pro	Tyr	Trp	Asp 100	Trp	Leu	Lys	Pro	Gln 105	Ser	Ala	Leu	Pro	Asp 110	Leu	Val
Thr	Gln	Glu 115	Thr	Tyr	Glu	His	Leu 120	Phe	Ser	His	Lys	Thr 125	Phe	Pro	Asn

72

<210> 78
 <211> 417
 <212> PRT
 <213> Megathura crenulata

<400> 78
 His Gly Ile Asn Val Arg His Val Gly Arg Asn Arg Ile Arg Met Glu
 1 5 10 15
 Leu Ser Glu Leu Thr Glu Arg Asp Leu Ala Ser Leu Lys Ser Ala Met
 20 25 30
 Arg Ser Leu Gln Ala Asp Asp Gly Val Asn Gly Tyr Gln Ala Ile Ala
 35 40 45
 Ser Phe His Gly Leu Pro Ala Ser Cys His Asp Asp Glu Gly His Glu
 50 55 60
 Ile Ala Cys Cys Ile His Gly Met Pro Val Phe Pro His Trp His Arg
 65 70 75 80
 Leu Tyr Thr Leu Gln Met Asp Met Ala Leu Leu Ser His Gly Ser Ala
 85 90 95
 Val Ala Ile Pro Tyr Trp Asp Trp Thr Lys Pro Ile Ser Lys Leu Pro
 100 105 110
 Asp Leu Phe Thr Ser Pro Glu Tyr Tyr Asp Pro Trp Arg Asp Ala Val
 115 120 125
 Val Asn Asn Pro Phe Ala Lys Gly Tyr Ile Lys Ser Glu Asp Ala Tyr
 130 135 140
 Thr Val Arg Asp Pro Gln Asp Ile Leu Tyr His Leu Gln Asp Glu Thr
 145 150 155 160
 Gly Thr Ser Val Leu Leu Asp Gln Thr Leu Leu Ala Leu Glu Gln Thr
 165 170 175
 Asp Phe Cys Asp Phe Glu Val Gln Phe Glu Val Val His Asn Ala Ile
 180 185 190
 His Tyr Leu Val Gly Gly Arg Gln Val Tyr Ala Leu Ser Ser Gln His
 195 200 205
 Tyr Ala Ser Tyr Asp Pro Ala Phe Phe Ile His His Ser Phe Val Asp
 210 215 220
 Lys Ile Trp Ala Val Trp Gln Ala Leu Gln Lys Lys Arg Lys Arg Pro
 225 230 235 240
 Tyr His Lys Ala Asp Cys Ala Leu Asn Met Met Thr Lys Pro Met Arg
 245 250 255
 Pro Phe Ala His Asp Phe Asn His Asn Gly Phe Thr Lys Met His Ala
 260 265 270

Asp	His	Ile	Ala	Gly	Ser	Gly	Val	Arg	Lys	Asp	Val	Thr	Ser	Leu	Thr
1				5					10					15	
Ala	Ser	Glu	Ile	Glu	Asn	Leu	Arg	His	Ala	Leu	Gln	Ser	Val	Met	Asp
			20					25					30		
Asp	Asp	Gly	Pro	Asn	Gly	Phe	Gln	Ala	Ile	Ala	Ala	Tyr	His	Gly	Ser
		35					40					45			
Pro	Pro	Met	Cys	His	Met	Xaa	Asp	Gly	Arg	Asp	Val	Ala	Cys	Cys	Thr
	50					55					60				
His	Gly	Met	Ala	Ser	Phe	Pro	His	Trp	His	Arg	Leu	Phe	Val	Lys	Gln
65					70					75					80
Met	Glu	Asp	Ala	Leu	Ala	Ala	His	Gly	Ala	His	Ile	Gly	Ile	Pro	Tyr
				85					90					95	
Trp	Asp	Trp	Thr	Ser	Ala	Phe	Ser	His	Leu	Pro	Ala	Leu	Val	Thr	Asp
			100					105					110		

His Glu His Asn Pro Phe His His Gly His Ile Ala His Arg Asn Val
115 120 125

Asp Thr Ser Arg Ser Pro Arg Asp Met Leu Phe Asn Asp Pro Glu His
130 135 140

Gly Ser Glu Ser Phe Phe Tyr Arg Gln Val Leu Leu Ala Leu Glu Gln
145 150 155 160

Thr Asp Phe Cys Gln Phe Glu Val Gln Phe Glu Ile Thr His Asn Ala
165 170 175

Ile His Ser Trp Thr Gly Gly His Thr Pro Tyr Gly Met Ser Ser Leu
180 185 190

Glu Tyr Thr Ala Tyr Asp Pro Leu Phe Tyr Leu His His Ser Asn Thr
195 200 205

Asp Arg Ile Trp Ala Ile Trp Gln Ala Leu Gln Lys Tyr Arg Gly Phe
210 215 220

Gln Tyr Asn Ala Ala His Cys Asp Ile Gln Val Leu Lys Gln Pro Leu
225 230 235 240

Lys Pro Phe Ser Glu Ser Arg Asn Pro Asn Pro Val Thr Arg Ala Asn
245 250 255

Ser Arg Ala Val Asp Ser Phe Asp Tyr Glu Arg Leu Asn Tyr Gln Tyr
260 265 270

Asp Thr Leu Thr Phe His Gly His Ser Ile Ser Glu Leu Asp Ala Met
275 280 285

Leu Gln Glu Arg Lys Lys Glu Glu Arg Thr Phe Ala Ala Phe Leu Leu
290 295 300

His Gly Phe Gly Ala Ser Ala Asp Val Ser Phe Asp Val Cys Thr Pro
305 310 315 320

Asp Gly His Cys Ala Phe Ala Gly Thr Phe Ala Val Leu Gly Gly Glu
325 330 335

Leu Glu Met Pro Trp Ser Phe Glu Arg Leu Phe Arg Tyr Asp Ile Thr
340 345 350

Lys Val Leu Lys Gln Met Asn Leu His Tyr Asp Ser Glu Phe His Phe
355 360 365

Glu Leu Lys Ile Val Gly Thr Asp Gly Thr Glu Leu Pro Ser Asp Arg
370 375 380

Ile Lys Ser Pro Thr Ile Glu His His Gly Gly
385 390 395

<210> 80
 <211> 1266
 <212> DNA
 <213> *Haliotis tuberculata*

<400> 80
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 aaggacgtga gtcacctcac ggatgacgag gtgcaagctc tccacggcgc cctccatgac 120
 gtcactgcat ctacagggcc tctgagtttc gaagacataa catcttacca tgccgcacca 180
 gcgctcgtgtg actacaaggg acggaagatc gcctgctgtg tccacgggtat gccagtttc 240
 cccttctggc acagggcata tgtcgtccaa gccgagcggg cactgttgctc caaacggaag 300
 actgtcggaa tgcccttactg ggactggacg caaacgctga ctacttacc atctcttgtg 360
 actgaaccca tctacattga cagtaaagggt ggaaaggctc aaaccaacta ctggtaccgc 420
 ggcgagatag cgttcatcaa taagaagact gcgcgagctg tagatgatcg cctattcgag 480
 aagggtggagc ctggtcacta cacacatctt atggagactg tctcgcacgc tctcgaacag 540
 gacgaattct gtaaatttga aatccagttc gagttggctc ataatgctat ccattacttg 600
 gttggcggta aatttgaata ttcaatgtca aacttggaat acacctccta cgaccccatc 660
 ttcttctctc accactccaa cgttgaccgc ctcttcgcca tctggcagcg tcttcaggaa 720
 ctgcgaggaa agaatcccaa tgcaatggac tgtgcacatg aactcgctca ccagcaactc 780
 caacccttca acagggacag caatccagtc cagctcacia aggaccactc gacacctgct 840
 gacctctttg attacaaaca acttggtatc agctacgaca gcttaaacct gaatggaatg 900
 acgccagaac agctgaaaac agaactagac gaacgccact ccaaagaacg tgcgtttgca 960
 agcttccgac tcagtggctt tgggggttct gccaacgttg ttgtctatgc atgtgtccct 1020
 gatgatgatc cacgcagtga tgactactgc gagaaagcag ggcacttctt cattcttggg 1080
 ggtcaaagcg aaatgccgtg gagattctac agacccttct tctatgatgt aactgaagcg 1140
 gtacatcacc ttggagtccc gctaagtggc cactactatg tgaaaacaga actcttcagc 1200
 gtgaatggca cagcactttc acctgatctt ctctctcaac caactgttgc ctaccgacct 1260
 gggaaa 1266

<210> 81
 <211> 1257
 <212> DNA
 <213> *Haliotis tuberculata*

<400> 81
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 atagatcatt tgactcgtga agaggaatac gagctaagga tggctctgga gagattccag 120
 gccgacacat ccgttgatgg gtaccaggct acagtagagt accatggcct tectgctcgt 180
 tgccacgac cagatgcaaa agtcagggtc gcctgttgta tgcattggat gccatccttc 240
 cctcactggc accggctgtt cggtacccag gtggaagatg ctcttgtagc gcgtggatcg 300
 cctatcgggtg ttcccttattg ggactggaca aaacctatga ctacacctcc agacttggca 360
 tcaaatgaga cgtacgtaga cccgtatgga catacacatc ataattcatt ctccaatgca 420
 aatatactct ttgaggaggg acaccatcac acgagcagga tgatagattc gaaactgttt 480
 gccccagtcg cttttgggga gcattcccat ctggttgatg gaatcctgta cgcatttgag 540
 cagggaagatt tctgcgactt tgagattcag tttgagttag tccataattc tattcatgag 600
 tggataggcg gttccgaaga ttactccatg gccaccctgc attacacagc ctttgacccc 660
 attttctacc ttcatcttc caatgtcgat cgtctatggg caatctggca agctcttcaa 720
 atcaggagac acaagccata tcaagcccac tgtgcacagt ctgtggaaca gttgccaatg 780
 aagccatttg ctttcccatc acctcttaac aacaacgaga agacacatag tcattcagtc 840
 ccgactgaca tttatgacta cgagggaagt ctgcactaca gctacgatga tctaactgtt 900
 ggtgggatga accttgaaga aatagaagaa gctatacatc tcagacaaca gcatgaacga 960
 gtcttcgcgg gatttctcct tgetggaata ggaacatctg cacttggtga cattttcata 1020
 aataaacggg ggaaccaacc actcaaagct ggagatattg ccattcttgg tgggtgccaag 1080
 gaaatgcctt gggcgtttga ccgcttgatg aaggtcgaaa taactgactc attgaagaca 1140
 ctttctctcg atgtcgatgg agattatgaa gtcactttta aaattcatga tatgcacgga 1200
 aacgctcttg atacggacct gattccacac gcagcagttg tttctgagcc agctcac 1257

<210> 82
 <211> 1242
 <212> DNA
 <213> *Haliotis tuberculata*

<400> 82
 cctacaccttg aggatgaaaa gcacagctta cgaatcagaa aaaatgtcga cagcttgact 60
 cctgaagaaa caaatgaact gcgtaaagcc ctggagcttc ttgaaaatga tcatactgca 120
 ggtggattca atcagcttgg cgccctccat ggagagccta aatgggtgcc taatcctgaa 180
 gcggagcaca aggttgcatt ctgtgttcat ggcatggctg ttttccctca ttggcacagg 240
 cttcttgctc tccaggcgga gaatgctctt agaaagcatg ggtacagtgg tgctctacca 300
 tactgggatt ggactcgccc cctttcccaa ctccctgac tggttagtca tgagcagtat 360
 acagatcctt ccgaccatca cgtgaagcat aaccctgtgt tcaatggcca catcgatata 420
 gtaaatacagg ataccaccag aagcgtacgg gaggatcttt atcaacaacc tgaatttgga 480
 catttcacgg atattgctca acaagtcctc ttagcattag aacaagatga cttctgttcg 540
 tttgaagtgc agtatgagat ttcccataat tttatccatg cacttgtagg aggaaccgac 600
 gcttatggca tggcatcgct gagatataca gcatacgatc caatcttttt cttgcatcat 660
 tcaaacaccg acaggatctg ggctatattg caatccctgc aaaaatacag aggcaaaccg 720
 tacaacactg ccaactgcgc catagaatct atgagaaggc ccctgcaacc atttggacta 780
 agcagtgcc aataacctga cagaatcacc agagagcatg ctatcccgtt tgatgtcttc 840
 aactatagag ataaccttca ttacgtatat gataccctgg aatttaattg tttgtcgatt 900
 tcacaacttg atagagagct ggaaaaaatc aagagtcacg aaagagtatt tgcctggattc 960
 ttgctgtcgg ggattaaaaa atctgctctt gtgaaattcg aagtttgtac tccacctgat 1020
 aattgtcata aagcagggga gttttatcta ctcggggacg aaaacgagat ggcttgggccc 1080
 tatgaccgac ttttcaagta tgatattact caggttctcg aagcaaacca tctacacttc 1140
 tatgatcatc tcttcattcg ctacgaagtc tttgatctta aaggagttag tttgggaact 1200
 gacctgttcc aacttgcaaa tgtggtacat gattccggca ca 1242

<210> 83
 <211> 1239
 <212> DNA
 <213> *Haliotis tuberculata*

<400> 83
 ggcacccgtg atcgtgataa ctacgttgaa gaagttactg gggccagtca tatcaggaag 60
 aatttgaacg acctcaatac cggagaaatg gaaagcctta gagctgcttt cctgcatatt 120
 caggacgacg gaacatatga atctattgcc cagtaccatg gcaaaccagg caaatgtcaa 180
 ttgaatgatc ataataattgc gtgttgtgtc catggtatgc ctaccttccc ccagtggcac 240
 agactgtatg tgggttcagggt ggagaatgct ctccataaca ggggatctgg tgtggctggt 300
 ccttactggg agtggactgc tcccatagac catctacctc atttcattga tgatgcaaca 360
 tacttcaatt cccgacaaca gcggtacgac cctaaccctt tcttcagggg aaaggttact 420
 tttgaaaacg cagtcacaac aagggaccca caagccgggc tcttcaactc agattatatg 480
 tatgagaatg ttttacttgc actggagcag gaaaattatt gtgactttga aattcagttt 540
 gagcttgctc ataacgcact tcattccatg ctgggaggta aagggcagta ctccatgtcc 600
 tccctggact attctgcgtt tgatcccgtc ttcttcctac atcatgcca cacggacaga 660
 ctgtgggcaa tctggcagga actacaaaga ttccgagaac tgcttatga agaagcgaac 720
 tgtgcaatca acctcatgca tcaaccactg aagccgttca gtgatccaca tgagaatcac 780
 gacaatgtca ctttgaaata ctcaaaacca caggacggat tcgactacca gaaccacttc 840
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 gaccgtttgt ataaatttga aatcaccaaa ccactgcaac agttaggagt caagctgcat 1140
 ggtggagttt tcgaactgga gcttgagatc aaggcataca acggttccta tctggatccc 1200
 catacctttg atccaactat catctttgaa cctggaaca 1239

78

<210> 86
<211> 1209
<212> DNA
<213> *Haliotis tuberculata*

<400> 86
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aacaccttga ctaaggctga gaccgacaac ctgagggagg cgctgtgggg tgtcatggca 120
gaccacggtc ccaatggctt tcaagctatt gctgctttcc atggaaaacc agcttttgtgt 180
cccatgcctg atggccacaa ctactcatgt tgtactcacg gcatggctac cttcccacac 240
tggcatcgcc tctacaccaa gcagatggag gatgcaatga gggcgcatgg gtctcatgtc 300
ggcctgccct actgggactg gactgctgcc ttcaccacc tgccaacact ggtcaccgac 360
acggacaaca accccttcca acatggacac attgattatc tcaatgtcag cacaactcga 420
tctccccgag acatgctgtt caacgacccc gagcatggat cagagtcggt cttctacaga 480
caagtcctct tagctctgga acaaactgat ttctgcaaat tcgaagtcca gtttgagata 540
accacaaatg ccatccattc ctggacaggt ggccacagcc cctacggaat gtccactctc 600
gacttcactg cctacgatcc tctcttctgg ctaccactc ccaacaccga cagaatctgg 660
gctgtctggc aagcttttga agaatacaga ggacttccat acaaccatgc caattgtgag 720
atccaggcaa tgaaaacgcc cctgaggcct ttcagtgcag atatcaacca caaccagtc 780
acaaaggcta acgcgaagcc attagatgtg ttcgagtata atcggttgag ttcaccagta 840
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aaggaggagg acagaatatt tgctgccttc cttctcagtg gaatcaagcg tagtgctgat 960
gtagtgttcg acatatgcca gccagaacac gaatgtgtgt tcgcagggac ttttgcgatt 1020
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aagtgatga agcagctaca cctgaggcat gactctgact ttaccttcag ggtgaagatt 1140
gtcggcaccg acgaccacga gcttccttca gacagtgtca aagcaccaac tattgaattt 1200
gaaccgggc 1209

<210> 87
<211> 1536
<212> DNA
<213> *Haliotis tuberculata*

<400> 87
gtgcacagag gcggaaacca cgaagatgaa caccatgatg acagactcgc agatgtcctg 60
atcaggaaag aagttgactt cctctccctg caagaggcca acgcaattaa ggatgcactg 120
tacaagctcc agaatgacga cagtaaaggg ggctttgagg ccatagctgg ctatcacggg 180
tatectaata tgtgtccaga aagaggtacc gacaagtatc cctgctgtgt ccacggaatg 240
cccggtgttc cccactggca ccgcctgcat accattcaga tggagagagc tctgaaaaac 300
catggctctc caatgggcat tccctactgg gattggacaa agaagatgtc gactcttcca 360
tctttctttg gagattccag caacaacaac ccttctaca aatattacat ccggggcggtg 420
cagcacgaaa caaccaggga cattaatcag agactcttta atcaaaccaa gtttggtgaa 480
tttgattacc tatattacct aactctgcaa gtccctggagg aaaactcgta ctgtgacttt 540
gaagttcagt atgagatcct ccataacgcc gtccactcct ggcttggagg aactggaaag 600
tattccatgt ctaccctgga gcattcgccc tttgacctg tcttcatgat tcaccactcg 660
agtttgagata gaatctggat cctttggcag aagttgcaaa agataagaat gaagccttac 720
tacgcattgg attgtgctgg cgacagactt atgaaagacc ccctgcatcc cttcaactac 780
gaaaccgtta atgaagatga attcaccgcg atcaactctt tcccaagcat actgtttgac 840
cactacaggt tcaactatga atacgataac atgagaatca ggggtcagga catacatgaa 900
cttgaagagg taattcagga attaagaaac aaagatcgca tatttgctgg ttttgttttg 960
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cacgaagaat atgcaggaga atttgcagtt ttgggagggt agaaggagat gccgtgggca 1080
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ctgtctcagc cattcatcgt ccaccgtcca gccatgtgg ctacacgacat cttggtaatc 1260
ccagtaggtg cgggccatga ccttcgcgct aaagtcgtag taaagagcgg caccaaagtc 1320
gagtttacac caatagattc gtcggtgaac aaagcaatgg tggagctggg cagctatact 1380

79

gctatggcta aatgcacgtg tccccctttc tttaccacg gctttgaact ggacaaagtc 1440
tacagcgctg atcacggaga ctactacatt gctgcaggta cccacgcgtt gtgtgagcag 1500
aacctcaggc tccacatcca cgtggaacac gagtag 1536

<210> 88

<211> 591

<212> DNA

<213> *Haliotis tuberculata*

<400> 88

ggtcttccgt actgggactg gacgcagcat ctgactcaac tcccagatct ggtgtcagac 60
cccttgtttg tgcacccgga aggaggaaag gcccatgaca acgcatggta tctgggaaac 120
atcaagtttg agaataagaa gactgcaaga gctggtgacg atcgctttt cgagaagggt 180
ggaccaggag agaatacccg actctttgaa ggaattctcg atgctcttga acaggatgaa 240
ttctgcaact tgcagatcca gtttgagttg gtcacaacg ctatccacta cctgggtggc 300
ggcgcgcaca cgtactccat gtctcatctc gactacacct cctacgacct cctcttcttc 360
ctccatcact ccaacccgga cgcactcttc gccatctggg aacgtcttca ggtactcaga 420
ggaaaggacc ccaacacgcg cgactgcgca cacaacctca tccatgagcc catggaaccg 480
ttccgtcggc atgagcccat ggaaccgttc cgtcgggact cgaacctct tgacctcacc 540
agggaaaact ccaaaccaat tgacagcttt gattatgccc accttggtta c 591

<210> 89

<211> 1245

<212> DNA

<213> *Haliotis tuberculata*

<400> 89

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catctgacac gcgaggaggt gtacgagctg cgcagagcta tggagagatt ccaggccgac 120
acatccgttg atgggtacca ggctacggtt gagtatcacg gcttacctgc tgcaggtcca 180
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gccacctata gagatcccat cagcggggac agcagacaca accccttcca cgatgttgaa 420
gttgcccttg aaaatggacg tacagaacgt caccagata gtagattgtt tgaacaacct 480
ttatttgga aacatacgcg tctcttcgac agtatagtct atgcttttga gcaggaggac 540
ttctgcgatt ttgaagttca atttgagatg acccataata atattcacgc ctggattggt 600
ggcggcgaga agtattccat gtcttctcta cactacacag ccttcgacct tatcttctac 660
cttcgtcact ccaacactga ccggctcttg gcaatttggc aagcgttgca gatacgaaga 720
aacaggcctt acaaggctca ttgtgcttg tctgaggaac gccagcctct caaaccttct 780
gccttcagtt cccactgaa caacaacgaa aaaactacg aaaactcgtt gccaccaaac 840
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ggatttgacc gtttgtacaa atatgagatt acagatgaac tgaggcaact taatctccgt 1140
gctgatgatg ttttcagcat ctctgttaaa gtaactgatg ttgatggcag tgagctgtcc 1200
tctgaactca tcccatctgc tgctatcatc ttcgaacgaa gccat 1245

<210> 90

<211> 1251

<212> DNA

<213> *Haliotis assimilis*

<400> 90

attgaccatc aggacccgca tcatgacaca atcattagga aaaatgttga taatcttaca 60
cccaggaaaa ttaattctct gaggcgggca atggcagacc ttcaatcaga caaaaccgcc 120

ggtggattcc	agcaaattgc	tgctttttcac	ggggaaccga	aatggtgccc	aagtcccgat	180
gctgagaaga	agttctcctg	ctgtgtccat	ggaatggctg	tcttcctca	ctggcacaga	240
ctcctgaccg	tgcaaggcga	gaatgcctg	agaaagcatg	gatgtctcgg	agctctcccc	300
tactgggact	ggactcggcc	cctgtctcac	ctacctgatt	tggttttggt	aagtagcaga	360
actacaccga	tgccatattc	caccgtggaa	gcccgaacc	cctggtacag	cggccatatt	420
gatacagttg	gtgttgacac	aacaagaagc	gtcctgcaag	aactgtatga	agctcctgga	480
tttggccatt	atactggggt	cgctaagcaa	gtgcttctgg	ctttggagca	ggatgacttc	540
tgtgattttg	aagtccagtt	tgagatagct	cacaatttca	ttcacgctct	tgtcggcgga	600
agcgagccat	atggtatggc	gtcactccgt	tacactactt	atgatccaat	tttctacctc	660
catcattcta	acactgacag	actctgggct	atatggcagg	ctctacaaaa	gtacaggggc	720
aaaccttaca	attccgccaa	ctgcgccatt	gcttctatga	gaaaaccctt	acaacctttt	780
ggtctgactg	atgagatcaa	cccggatgat	gagacaagac	agcatgctgt	tcctttcagt	840
gtctttgatt	acaagaacaa	cttcaattat	gaatatgaca	cccttgactt	caacggacta	900
tcaatctccc	agctggaccg	tgaactgtca	cggagaaagt	ctcatgacag	agtattttgcc	960
ggatttttgc	tgcatgggat	tcagcagctc	gcactagtta	aattctttgt	ctgcaaatca	1020
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ccatggggct	atgatcgtct	ttacaaatat	gagatcactg	agcagctcaa	tgccctggat	1140
ctacacatcg	gagatagatt	cttcatcaga	tacgaagcgt	ttgatcttca	tggtacaagt	1200
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<210> 91

<211> 1242

<212> DNA

<213> Haliotis tuberculata

<400> 91

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<210> 92

$\langle 211 \rangle$ 1257

<212> DNA

<213> Haliotis tuberculata

<400> 92

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81

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<210> 93

<211> 1248

<212> DNA

<213> *Haliotis tuberculata*

<400> 93

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<210> 94

<211> 1206

<212> DNA

<213> *Haliotis tuberculata*

<400> 94

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82

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<210> 95

<211> 1548

<212> DNA

<213> *Haliotis tuberculata*

<400> 95

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<210> 96

<211> 966

<212> DNA

<213> *Megathura crenulata*

<400> 96

83

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<210> 97
 <211> 1242
 <212> DNA
 <213> Megathura crenulata

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<210> 98
 <211> 1236
 <212> DNA
 <213> Megathura crenulata

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84

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<210> 99

<211> 1257

<212> DNA

<213> Megathura crenulata

<400> 99

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<210> 100

<211> 1254

<212> DNA

<213> Megathura crenulata

<400> 100

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85

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<212> DNA

<213> Megathura crenulata

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<212> DNA

<213> Megathura crenulata

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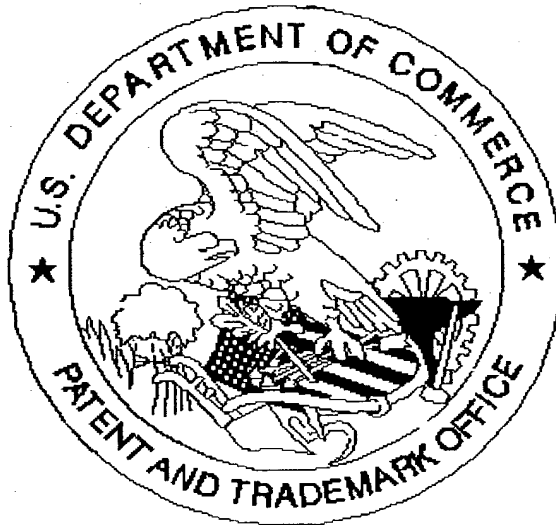
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